HEALTH CENTER LIBRARY

BRITISH MEDICAL JOURNAL

JOURNAL OF THE BRITISH MEDICAL ASSOCIATION

SATURDAY AUGUST 29 1959

TABLE OF CONTENTS

Significance of Respiratory Symptoms and the Diagnosis of Chronic Bronchitis in a Working Population C. M. FLETCHER, M.D., F.R.C.P., P. C. ELMES, B.M., M.R.C.P., A. S. FAIRBAIRN, M.B., and C. H. WOOD, M.B., D.P.H. 257

Secretion of Blood-group Substances in Rheumatic Fever A. A. GLYNN, M.B., M.R.C.P., L. E. GLYNN, M.D., M.R.C.P., and E. J. HOLBOROW, M.D. 266

Anterior Tibial Syndrome Due to Arterial Embolism and Thrombosis BERNARD J. FREEDMAN, M.B., M.R.C.P., and C. H. R. KNOWLES, M.D. 270

Hypercalcaemia and Renal Failure in Multiple Secondary Carcinoma of Bone P. H. SANDERSON, M.B., M.R.C.P. ...275

Breast Abscess as a Threat to Surgical Units in a General Hospital J. G. P. HUTCHISON, M.D. 277

Treatment of Tuberculosis of the Spine M. C. WILKINSON, M.B., F.R.C.S. 280

Stanleyville I and II PAULETTE DHERTE, J. VANDEPITTE, M.D., J. A. M. AGER, M.B., and H. LEHMANN, M.D., SC.D., M.R.C.P., F.R.I.C. 282

A New Haemoglobin Variant in an American Negro ROSE G. SCHNEIDER, PH.D., and MARY ELLEN HAGGARD, M.D. 285

Griseofulvin Treatment of Acute Cattle Ringworm Infections in Man THOMAS COCHRANE, M.D., F.R.F.P.S., and ADAM TOSZEVIC, M.D., Ch.M. 286

MEDICAL MEMORANDA

Calcified Subphrenic Abscess. A. C. G. KHUAN, M.B., B.S. 287

BOOK REVIEWS 289

GENERAL ARTICLES AND NEWS

Annual Meeting, Edinburgh:
First Plenary Session 297
Second Plenary Session 297
General Session 298
To-day's Drugs 300
NEW APPLIANCES 299
MEDICO-LEGAL 312
UNIVERSITIES AND COLLEGES 313
VITAL STATISTICS 313
MEDICAL NEWS 315
BIRTHS, MARRIAGES, AND DEATHS 316
QUESTIONS AND COMMENTS 317

OBITUARY

Sir Robert Young, C.B.E., M.D., F.R.C.P. ..307
J. Norris Whyte, M.D., D.P.H. 309
C. P. Rhoads, M.D., D.SC. 309
A. Ruscoe Clarke, M.B.E., M.B., F.R.C.S. ..310
W. A. S. Lamborn, O.B.E., M.R.C.P. 310
R. S. C. McDade, M.B., B.Chir. 311
J. D. Sinclair, O.B.E., M.R.C.S., L.R.C.P. ..311
R. C. L'Estrange Burges, M.B., B.Chir. ..311

LEADING ARTICLES

Oncogenic Particles 291
Coxsackie Infection of Cows 292
Support for Cancer Research 293

ANNOTATIONS

Cet Animal est Mechant 294
Leucocyte Agglutinins 295
Disposal of Radioactive Waste 295
Living in Caravans 296

CORRESPONDENCE

B.C.G. Vaccination. H. G. CALWELL, M.D.; R. S. DOIG, M.B., D.P.H. 300
Jejunal Diverticulosis with Megaloblastic Anaemia. E. MONTUSCHI, M.D. 301
Telling the Cancer Patient. A. NORMAN LEEMING, M.B. 302
Inhibition of Lactation. A. P. CAMILLERI, M.D., D.Obst.R.C.O.G. 302

SUPPLEMENT

Full Contents on First Page of Supplement
Annual Representative Meeting, Edinburgh, 1959 53
Labour Party's Health Policy 66
Correspondence:
Doctors on Probation. A. J. BAIN, D.P.M. 66

CORRESPONDENCE—*contd.*

Haemarthrosis. N. TREVOR BURNETT, M.B. 302
Chlorothiazide and Hydrochlorothiazide. R. LL. LYON, M.B. 302
Purpura in Kwashiorkor. Z. A. LEITNER, M.D. 303
The Occasional Obstetrician. DOREEN S. BALL, D.Obst.R.C.O.G. 303
Sterile Syringe Service for General Practitioners. G. BEHR, M.R.C.P. 304
Peptic Ulcer in Africans. B. J. BALDACHIN, M.R.C.P.Ed., and P. E. S. PALMER, F.F.R.; PETER KONSTAM, F.R.C.S.Ed. 304
Multiplication of Trade Names. G. F. WALKER, M.D. 305
Adoption Act. W. H. DICKINSON PRIEST, M.R.C.S. 305
Anaesthesia for Bronchoscopy. P. K. CHANDRASEKARAN, M.B. 305
Quarantine Outmoded. Sir GEORGE W. PICKERING, F.R.C.P. 305
Inoculation Recording by Tattooing. L. B. SCOTT, F.R.C.S.Ed.; H. J. PARISH, F.R.C.P.Ed. 306
Water Intoxication. E. CLAYTON-JONES, M.D. 306
Influenza. M. CURWEN, M.B. 306
Letters on other subjects appear on p. 307

OHIO STATE UNIVERSITY LIBRARY

BRITISH MEDICAL ASSOCIATION, TAVISTOCK SQUARE, LONDON, W.C.1

No. 5147, WEEKLY, PRICE 3/-

Copyright © 1959

REGISTERED AS A NEWSPAPER

ASTHMA

Rely on Rybar for Instant Relief

Ever increasing numbers of medical men are relying on Rybarvin Inhalant to combat broncho-spasm. The Ministry of Health have agreed to the prices of Rybar asthma inhalants.

RYBARVIN brings relief. Consistently, often spectacularly, attacks are cut short and their frequency lessened. Free from excess acid, non-irritant and non-habit-forming, it is an ideal inhalant for all asthmatics, young and old.

Formula

Pituitary Extract. Posterior and Anterior Lobe	0·40% w/v
Methylatropine Nitrate	0·14% w/v
Papaverine	0·08% w/v
Adrenaline	0·40% w/v
Ethyl Para-aminobenzoate	0·20% w/v
Iso-butyl Para-aminobenzoate	0·01% w/v

RYBAR INHALER has been specially designed for aerosol therapy.

Both Rybarvin and the Inhaler may be prescribed on N.H.S. Form E.C.10.

Samples and details of trial outfits forwarded on request.

TANKERTON **RYBAR** KENT

LABORATORIES LTD.

F283

THE WORLD'S GREATEST BOOKSHOP

FOYLES

++FOR BOOKS++

BIG DEPARTMENT FOR

Medical Books

Many medical men tell us that it is the best Medical Book Department in London

119-125 CHARING CROSS RD., LONDON, W.C.2

Gerrard 5660 (20 lines). Open 9-6 (*inc. Sats.*)

Two minutes from Tottenham Court Road Station

SPECIALIST JOURNALS

ANNALS OF THE RHEUMATIC DISEASES
BRITISH HEART JOURNAL
BRITISH JOURNAL OF INDUSTRIAL MEDICINE
BRITISH JOURNAL OF PREVENTIVE AND SOCIAL MEDICINE
BRITISH JOURNAL OF VENEREAL DISEASES
JOURNAL OF NEUROLOGY, NEUROSURGERY AND PSYCHIATRY
MEDICAL AND BIOLOGICAL ILLUSTRATION
THORAX
Quarterly. Annual Subscription £3 each.
ARCHIVES OF DISEASE IN CHILDHOOD
JOURNAL OF CLINICAL PATHOLOGY
Bimonthly. Annual Subscription £4 4s.
BRITISH JOURNAL OF PHARMACOLOGY AND CHEMOTHERAPY
Quarterly. Annual Subscription, £4 4s.
BRITISH JOURNAL OF OPHTHALMOLOGY
Monthly. Annual Subscription, £6.
OPHTHALMIC LITERATURE
Six issues and index yearly. Annual Subscription, £4 4s.
Combined subscription with British Journal of Ophthalmology, £9.

BRITISH MEDICAL ASSOCIATION

B.M.A. House, Tavistock Square, London, W.C.1

PM

NUTRITION AND THE PUBLIC HEALTH

H. E. MAGEE, M.B., B.Ch., D.Sc., M.R.C.P.

Formerly Senior Medical Officer (Nutrition), Ministry of Health

The author is well known as a nutrition expert. He has been concerned with food and nutrition for more than forty years and was responsible for nutrition at the Ministry of Health during the war. This short and readable book is the essence of his considerable experience. It will be invaluable for all concerned with nutrition, public health workers and medical and nursing students. 25s. net.

VIRAL AND RICKETTSIAL INFECTIONS OF MAN

Edited by THOMAS M. RIVERS, M.D., and FRANK L. HORSFALL, M.D.

The new third edition of this well-known standard work has been practically rewritten in the light of the remarkable changes in this field. Virtually a new and completely up-to-date book, it still retains the stamp of the success and authority of previous editions. £3 3s. net.

PITMAN MEDICAL PUBLISHING CO. LTD.

39 Parker Street . London . W.C.2

ANY QUESTIONS?

Second Series. ● Third Series—with Cumulative Index

Price 7s. 6d. each (by post 8s. 3d.)

These pocket-size volumes each contain some 200 questions and expert answers from the "Any Questions?" pages of the *British Medical Journal*. Each answer has been chosen for its practical value to doctors in their day-to-day work. Many deal with subjects not covered in the standard textbooks.

The Third Volume has a cumulative index to all the answers appearing in the three books in the series.

Obtainable from booksellers or by post from Publishing Manager

BRITISH MEDICAL ASSOCIATION

B.M.A. House, Tavistock Square, London, W.C.1

or from Regional Offices of the Association

BRITISH MEDICAL JOURNAL

LONDON SATURDAY AUGUST 29 1959

THE SIGNIFICANCE OF RESPIRATORY SYMPTOMS AND THE DIAGNOSIS OF CHRONIC BRONCHITIS IN A WORKING POPULATION

BY

C. M. FLETCHER, C.B.E., M.D., F.R.C.P.
Senior Lecturer in Medicine, Postgraduate Medical School of London

P. C. ELMES, B.M., M.R.C.P.
Senior Registrar, Hammersmith Hospital, London

A. S. FAIRBAIRN, M.B.
Member, Statistical Research Unit, Medical Research Council; Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine, London

AND

C. H. WOOD, M.B., B.S., D.P.H.
Lecturer in Occupational Health, London School of Hygiene and Tropical Medicine

The difficulty of defining "chronic bronchitis" has been referred to in many recent publications (Higgins *et al.*, 1956; Stuart-Harris and Hanley, 1957; Oswald, 1958). One essential feature of the disease, upon which Scadding (1952) based his definition, is "chronic or recurrent cough with expectoration," but there is no agreement upon where the line should be drawn between "the earliest phase of the disease and health" (*British Medical Journal*, 1959); nor has it been shown that any such line can be drawn by simple symptomatic inquiry, without the gross observer variation first described by Cochrane *et al.* (1951).

We have investigated this diagnostic problem by asking working men and women in London a number of questions about cough, expectoration, and other symptoms. The same subjects were asked these questions on two occasions, and the validity and significance of their replies were tested by comparison with measurements of sputum volume, ventilatory capacity, and sickness absence rates. Fairbairn *et al.* (1959) discuss elsewhere the variation that was found between the answers obtained by the three doctors and three nurses who asked the questions, and they suggest means of reducing this variation. The errors found were not so great as to preclude the use of the method for survey purposes.

In this paper we are concerned with the prevalence of symptoms in the men and women we studied and with the relationship of these symptoms to one another and to the results of the more objective tests. We propose a definition of chronic bronchitis and suggest simple combinations of questions and tests by which the disease may be diagnosed.

Methods

Fairbairn *et al.* describe the selection of subjects and the questionary that was used. The parts of the questionary referred to in the present paper are given in the Appendix. The men, aged 40–59, were postmen attached to the East Central Divisional Office of the General Post Office in the City of London. The women, also aged 40–59, were engaged in sorting documents in the Post Office Savings Branch of the General Post Office in West London. 192 subjects of each sex were interviewed on the first occasion, and 144 of these were interviewed on the second occasion. Elmes *et al.* (1959) have described how sputum specimens were collected and examined. These specimens were collected from the men in February, March, and August, and from the women in March and August, and consisted of the sputum brought up in the first hour after rising.

Measurements of the one-second forced expiratory volume ($F.E.V._1$) (Gandevia and Hugh-Jones, 1957) were derived from tracings of expirations made on a light spirometer with a paper speed of 2 cm./sec. They were corrected to body temperature and saturation, and, for some purposes, were standardized to age 40 from the regression relationship with age, using those subjects who denied cough, sputum, and breathlessness. The results were multiplied by 35 and expressed as indirect maximum breathing capacity (M.B.C.), since this correction has been widely used in epidemiological surveys in this country, and the normal values of the M.B.C. are more generally known than for those of the $F.E.V._1$. The sickness absence records of each subject for the previous three years were inspected, and all absences lasting more than one week with a diagnosis of influenza, bronchial catarrh, and bronchitis were considered to be "chest illnesses." These were recorded for comparison with chest illnesses reported by the subject during this period.

Prevalence of Respiratory Symptoms

Cough and Phlegm.—In recording replies to questions 1–10 on cough and phlegm the interviewers were instructed to record as positive only cough or phlegm which occurred "on most days for at least three months every year." Table I shows that about half the men

TABLE I.—*Percentage of Positive Answers to Questions at First Interview*

Question		Men			Women		
		Aged 40–49	Aged 50–59	All Ages	Aged 40–49	Aged 50–59	All Ages
1	Cough, usually	24	37	30	21	17	19
2	,, on rising, winter	42	54	48	27	21	24
3	Cough on rising, summer	26	39	32	18	7·5	12·5
2+4	Cough all day, winter	14·5	20	17	12·5	5	9
2+5	Cough all day, summer	8·5	11·5	10	6·5	3	4·5
6	Phlegm usually	31	47	39	20	18	19
7	,, on rising, winter	29	47	38	22	22	22
8	Phlegm on rising, summer	18	32	25	14·5	8.5	11·5
7+9	Phlegm all day, winter	8·5	25	16·5	6·5	4	5
7+10	Phlegm all day, summer	5	13·5	9·5	3	2	2·5
17	Dyspnoea grade 1 (no dyspnoea)	90	64	77	73	68	70
	Dyspnoea grade 2	8	20	14	22	26	24
	,, ,, 3	2	14	8	4	5	4·5
	,, ,, 4 and 5	—	2	1	1	1	1
22	Wheeze occasionally	47	50	48·5	49	45	47
23	Wheeze most days or nights	10·5	20	15	8·5	6·5	7·5
29	Colds usually go to chest	31	37	34	36	40	38
31	Chest affected by weather	31	41	36	25	25	25
31+38	Chest affected by weather, with breathlessness	20	28	24	19	21	20
41	Nasal catarrh: winter	37	47	42	35	29	32
42	Nasal catarrh: summer	23	27	25	18	19	18·5
43+43a	Chest illnesses*: only 1	25	15	20	29	21	25
	Chest illnesses*: 2 or more	13	25	19	23	33	28

* Excluding illnesses stated to be less than 1 week in duration.

and a quarter of the women had morning cough; rather fewer admitted to phlegm. As would be expected, cough and production of phlegm was more commonly recorded on rising than during the day and in winter than in summer in both sexes. The prevalence of positive answers to the less specific questions (1 and 6), "Do you usually have cough/phlegm?" (used by Higgins *et al.*, 1956; Higgins, 1957), roughly corresponded to that of "cough on rising in winter and summer" and of "production of phlegm on rising in the winter" respectively. While the prevalence of each grade of symptom was higher in the older than in the younger men, the reverse was true in the women.

Most of the cough and phlegm reported could be regarded as chronic; for only 5% of all subjects with cough or phlegm said that these symptoms had been present for more than three years (Question 16).

Breathlessness on Exertion.—Subjects were classified into five grades of breathlessness on their replies to questions (17) similar to those described by Fletcher (1952). As with cough and sputum, there was a significantly greater prevalence of breathlessness in the older than in the younger men but no trend with age in the women. The net effect was a similar prevalence in the two sexes, with a slight but not significant excess of grades 3 and over in the men compared with the women.

Other Symptoms.—Nearly half of both the men and women of all ages admitted to occasional wheezing, chiefly with colds. Significantly more men than women admitted to wheezing "most days or nights," and here, too, the prevalence was greater in the older men. There is little sex or age effect in the proportion of subjects who said that colds went to their chests. Rather more men than women said the weather (chiefly fog) affected their chest and that adverse weather caused dyspnoea—again a slight age differential is apparent in the men but not the women. Positive replies to the question "Do you usually have a stuffy nose or catarrh at the back of your nose?" were frequent. This symptom was nearly twice as prevalent in winter as in summer, again with a slightly higher prevalence and an age effect in the men. Chest illnesses were of similar prevalence in the two sexes. The older subjects of both sexes had more frequent illnesses.

In summary, chest symptoms were prevalent in both men and women. The chief difference between the sexes was that for nearly every symptom the prevalence rose with age in the men but not in the women. Only cough and phlegm were significantly more prevalent in the men as a whole than in the women. These differences are discussed below.

Symptoms in Relation to Objective Measures.—Chronic cough and sputum, with recurrent chest illness and breathlessness on exertion, are chief complaints upon which chronic bronchitis is customarily diagnosed, and we have related these symptoms to observations made on the sputum specimens, records of sickness absence from chest diseases, and ventilatory capacity (estimated by indirect M.B.C.).

Phlegm Production

The replies on phlegm production rather than on cough are considered because the former are more relevant to the sputum specimens. The replies to questions on cough and phlegm were closely related. Of 62 men who denied any phlegm at the second

TABLE II.—*Relationship Between Answers to Questions about Phlegm Production and Winter Sputum Volumes, Indirect M.B.C. (standardized to age 40) and Other Symptoms. Men: Second Interview*

Time at which Phlegm Production Admitted	No. of Men	No. of Sputum Bottles Returned*	Percentage of Bottles, with Sputum Volumes:				Mean Indirect M.B.C. (l./min.)	Symptom Marks† (% Possible)
			Nil	<2 ml.	2–6 ml.	>6 ml.		
No phlegm	62	105	75	16	7	2	117	10
On rising only	30	48	23	40	27	10	112	20
During day ,,	16	26	35	38	15·5	11·5	110	26
Part ,, ,,	46	74	27	39	23	11	111	22
On rising and during day	36	68	16	15	36	33	93	52
Winter only	31	54	30	24	31·5	14·5	100·5	32
All year	51	87	17·5	30	27·5	25	107·5	38
"Usually" (question 6)	60	100	16	23	32	29	102	41

* Two possible winter specimens per man

† One mark for dyspnoea grade 2, wheeze most days, weather affects chest without dyspnoea, 1 chest illness. Two marks for dyspnoea grade 3, weather causes dyspnoea, 2 or more chest illnesses.

interview, only 12 (19%) said they coughed, while of 59 men who denied any cough, only 9 (15%) said they produced phlegm. Five questions about phlegm production were used to grade its severity. The prevalence of positive answers to these questions (Table I) suggests that such a grading might be based either on the time of the day or on the time of the year during which phlegm was produced, or on both. We have tried to see which is the more valid by the relationship of positive answers to the volume of sputum and the indirect M.B.C. We deal with the answers given by the men (because of their greater frequency of positive replies) at the second interview (because on the first occasion questions about cough and phlegm during the day were asked only if they had occurred on rising, so that subjects coughing or expectorating only during the day were missed). In Table II the men are grouped according to the time of day and year at which they said they produced phlegm.

The questions referred to the usual habit "for most days for at least three months each year." A subject who "usually" produced phlegm might naturally fail to do so on the two particular days when the specimens were collected. Conversely, a subject "usually" free from phlegm might have a short period of productive cough. Thus it is not surprising that 25% of those who denied phlegm produced sputum, mostly in small amounts. 23% of the subjects who said they had morning phlegm returned empty bottles. In a few of these subjects there is indirect evidence that this may have been due to failure to co-operate (Elmes *et al.*, 1959).

The distribution of winter sputum volumes is very significantly different ($P<0.001$) in three groups of men: those who denied phlegm, those who admitted to it for only part of the day (only on rising or only later on), and those who admitted to it throughout the day. There is, however, a negligible difference ($P=0.7$) between those who admitted to phlegm only on rising and those who admitted to it only later in the day. Similarly, there is no significant difference between those who admitted to phlegm only in the winter and those who admitted to it throughout the year ($P=0.2$).

It appears, therefore, that subjects who denied phlegm, those who noticed it on rising or later in the day only, and those who noticed it both on rising and throughout the day are three groups characterized by progressively greater sputum volumes in the first hour after rising. This presumably indicates increasing degrees of bronchial hypersecretion. Classification of our subjects according to the time of year or time of day when the phlegm was experienced gives no additional information.

The three groups of subjects also show a downward trend in the mean values of the M.B.C. The mean value of those denying phlegm (117) is slightly but not significantly higher than those with phlegm for part of the day only (111), but the mean of each of these groups is significantly higher than the mean of those with phlegm throughout the day (93). The mean values of those with phlegm in the winter only (100.5) and with phlegm throughout the year (107.5) do not differ significantly.

Although not an objective criterion, the frequency of other symptoms assessed on an arbitrary system of marking (shown in the last column of Table II) also supports this threefold classification. The differences between these three classes of men according to the three criteria we have chosen are illustrated in Fig. 1.

The apparent similarity of those with winter and those with perennial phlegm is surprising, since it is often thought that a winter cough represents an earlier stage of chronic bronchitis than a perennial cough. The explanation appears to be that recollection of summer phlegm production was inaccurate in our

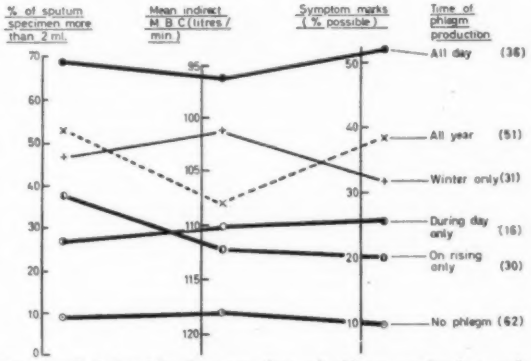

% of sputum specimen more than 2 ml.
Mean indirect M.B.C (litres / min.)
Symptom marks (% possible)
Time of phlegm production
All day (36)
All year (51)
Winter only (31)
During day only (18)
On rising only (30)
No phlegm (62)

FIG. 1.—Relationships between time of phlegm production and volume of winter sputum, indirect M.B.C., and other symptoms.

subjects, who were questioned during the winter. It is shown in Table III that 40% of those who said they produced phlegm only in winter produced specimens of the same mean volume in summer. The proportion of men who produced specimens of sputum in summer was only just significantly less in those who denied than in those who admitted to summer phlegm. Thus questions on seasonal changes in phlegm production do not produce answers reliable enough to be worth asking.

When the subjects are divided into three groups either by the questions or by measurement of sputum volumes (Table IV) there is a highly significant correlation

TABLE III.—*Replies to Questions on Phlegm Production in Winter and Summer Compared with Sputum Specimens. Men and Women Combined*

Replies to Questions on Phlegm	Percentage of Returned Bottles Containing Sputum		Mean Volume of Sputum (ml.)†	
	Winter*	Summer	Winter*	Summer
Phlegm only in winter ..	69	40	4·1	4·0
,, winter and summer	72	64	5·0	3·8

* February specimen for men, March for women.
† Excluding empty bottles.

TABLE IV.—*Relationship Between Grades of Expectoration Based on Answers to Questions and on Measurements of Winter Sputum Volumes. (Men: Second Interview. Two Winter Specimens Combined. Women: First Interview)*

Sex	Answers to Phlegm Questions	Sputum Volume			Total
		Nil	<2 ml.	2 ml.+	
Men	No phlegm ..	79	17	9	105
	Phlegm part of day	20	29	25	74
	,, all day ..	11	10	46	67
	Total ..	110	56	80	246
Women	No phlegm ..	124	14	5	143
	Phlegm part of day	19	11	9	39
	,, all day ..	3	6	1	10
	Total ..	146	31	15	192

WELLCOME INSTITUTE LIBRARY

($P<0.001$) between the two methods in both sexes, but the sputum volumes place rather more subjects in the most abnormal group. Table V shows that the two methods have similar repeatability, placing 76% and 72% of the subjects respectively into the same groups on the two occasions.

TABLE V.—*Repeatability of Grading of Expectoration by Answers to Questions and by Measuring Sputum Volumes: Men*

Answers at First Interview	Answers at Second Interview			Total
	No Phlegm	Phlegm Part of Day	Phlegm All Day	
No phlegm ..	58	13	3	74
Phlegm part of day	4	15	8	27
,, all day ..	—	2	25	27
Total ..	62	30	36	128*
Volume of Sputum in February	Volume of Sputum in March			Total
	Nil	<2 ml.	2 ml.+	
Nil	46	10	5	61
<2 ml.	6	18	8	32
2 ml.+	4	6	35	45
Total ..	56	34	48	138†

* Omitting 16 men who admitted to phlegm only later in the day since these were missed at first interview (see text).
† 54 men failed to return sputum bottles on one or other occasion.

We have assumed that the phlegm to which our subjects admitted and the sputum they produced came from their bronchi and not from their sinuses. In the questions about phlegm the interviewers were instructed to emphasize the words "from your chest," and the words "not from the back of your nose" were inserted to attempt to exclude nasal secretions. In both men and women the frequency of winter nasal catarrh (question 41) was twice as great in those who said they produced phlegm as in those who denied it, and it was more frequent in those with greater volumes of sputum than in those with smaller volumes. This association of phlegm production with nasal catarrh was similar in degree to its association with other symptoms such as dyspnoea, colds going to the chest, and chest illnesses. It seems more likely that there is a real association between nasal and bronchial catarrh than that the two were confused. We believe that our questions and our instructions concerning the sputum specimens were such that we were concerned predominantly with bronchial and not nasal secretions.

We conclude that asking questions and collecting sputum provide two similar, reasonably repeatable methods of grading the amount of expectoration. Sputum collection is more objective, but demands co-operation in a procedure which is troublesome and may be distasteful. Moreover, it is liable to error in collection and to the effects of variations in sputum volume during a transient chest infection. The questions are perhaps more relevant to the chronic condition in which we are interested, and are easy to ask; but they are liable to the observer variation described by Fairbairn *et al.* (1959), which renders uncertain comparisons between surveys carried out by different observers (see Table XII).

There is a significant but not very close association between the replies to questions about the colour of the phlegm and purulence of sputum specimens. 50% of the sputum specimens were mucopurulent in those who said their phlegm was "always white, grey, or black," but 80% in those who said it was sometimes or always yellow.

Chest Illnesses

Elmes *et al.* (1957) found that out-patients with chronic bronchitis tended to exaggerate the number and duration of past sickness absences from work owing to chest illness. We therefore compared our subjects' accounts of their chest illnesses with their sickness absence records. In the questionary a simple question (43) about chest illnesses which had kept the subjects off work was first asked, and if this was negative a supplementary question (43a) was asked ("not even 'flu ?") to stimulate the memory. In Table VI the illnesses remembered as the result of the first question are compared with the sickness absence records.

In the men the correspondence is quite good, but is enhanced by the high proportion with no illnesses. There is only 37% agreement in those who either admitted to or had a record of a chest illness. There is, however, no evidence that answers to questions exaggerated the number of illnesses. The supplementary question elicited 12 more illnesses, the inclusion of which did not affect the agreement with the records. In the women the agreement between recollected and recorded illnesses is less good and there are more of the latter. 26 further illnesses were recalled in answer to the supplementary question, but their inclusion did not improve the agreement. 78% of the women were married, and it is not unlikely that some of their recorded absences were due to domestic cares rather than to actual illness. There was no reduction of mean indirect M.B.C. in those subjects of either sex who reported illnesses only in answer to the extra question, which does not appear to be worth asking.

TABLE VI.—*Comparison Between Sickness Absence Records for Chest Illnesses and Illnesses Reported in Answer to Question* 43

No. of Chest Illnesses Reported in Answer to Question	No. of Chest Illnesses from Sickness Absence Records							
	Men				Women			
	None	1 Only	2 or More	Total	None	1 Only	2 or More	Total
None	93	14	5	112	56	31	15	102
1 only	10	12	4	26	9	9	7	25
2 or more ..	7	7	16	30	10	5	24	39
Total ..	110	33	25	168	75	45	46	166

Correct replies for men = 121/168 = 72%.
,, ,, ,, women = 89/166 = 54%.

There was thus no marked tendency to exaggerate or forget past illnesses. Indeed, the correspondence between recollected and recorded illnesses is surprisingly close in view of the difficulty of deciding from the sickness records what should be counted as a chest illness.

Breathlessness and Indirect M.B.C.

Measurements of the indirect M.B.C. were made upon all but one of the men at the second interview, giving 143 readings. Measurements were made on all but five of the women at the first interview, giving 187 readings. The missing readings were due to five subjects who objected to the procedure and to one technical error.

Fig. 2 shows the frequency distribution of the M.B.C. in men and women. There were a few men with greatly impaired ventilatory capacity who produce a skewing of the distribution to the left. If men admitting to phlegm throughout the day are excluded, a relatively normal distribution is obtained. The mean values are then 113.5 for men and 97 for women, with coefficients of variation of 18.6 and 14.2 respectively. There are only two women but 11 men with M.B.C.s more than two standard deviations below this mean; 10 of these men admitted to phlegm throughout the day, and one to phlegm on rising only, but the two women denied any phlegm.

The indirect M.B.C. correlates poorly with the answers to questions on dyspnoea (Table VII). There was only a slight depression of mean M.B.C. in association with dyspnoea in the men and none at all in the women. As the test measures only reduction in ventilatory capacity and has no relation to other disturbances of pulmonary or cardiac function that may cause dyspnoea, it is perhaps not surprising that several subjects who said that they had to walk slowly on the level because of dyspnoea (grade 3 or more) had indirect M.B.C.s within 1 S.D. of the mean. It is, however, surprising that, of the 11 men with an indirect M.B.C. more than 2 S.D. below the mean, four denied any dyspnoea (including one man with a value of 22.5 l./min.). Questions about dyspnoea appear to provide a poor indication of impairment of lung function in association with bronchitis. The indirect M.B.C. is reduced by obstruction to bronchial air flow, which is the aspect of lung function that would be expected, on theoretical grounds, to be specifically impaired in bronchitis, and it is an objective, repeatable, and simple test.

Other Symptoms and Indirect M.B.C.

A significant depression of M.B.C. occurs in men who admitted to cough or phlegm throughout the day, to wheeze most days and nights, to adverse weather causing dyspnoea, to having had two or more chest illnesses or one or more illnesses with increased phlegm production. The depression of M.B.C. is in each case largely due to the same 11 men, mentioned above, 10 of whom had three or more of these severer symptoms. If these men are excluded, the mean M.B.C. of the remainder is less markedly yet still consistently depressed in each of these symptom categories.

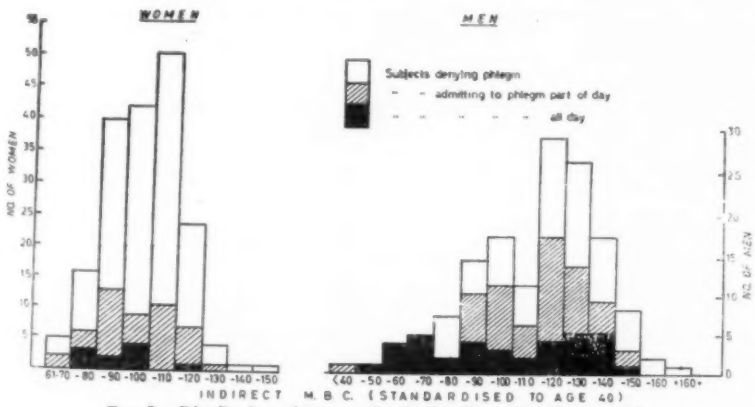

WOMEN
MEN
Subjects denying phlegm
admitting to phlegm part of day
all day
NO. OF WOMEN
NO. OF MEN
61-70 -80 -90 -100 -110 -120 -130 -140 -150
(40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 +160+
INDIRECT M.B.C. (STANDARDISED TO AGE 40)

FIG. 2.—Distribution of age-standardized indirect M.B.C. (l./min.).

TABLE VII.—*Relationship Between Age-standardized M.B.C. and Various Symptoms; Men and Women. First Questionary*

Symptom Group		Men				Women	
		No.	Mean Indirect M.B.C. (l./min.) All Cases	Excluding 11 Low Values No.	Excluding 11 Low Values Mean	No.	Mean Indirect M.B.C. (l./min.)
Cough*	None	58	117	58	117	136	98
	On waking *or* later in day	54	112	52	114	33	94
	On waking *and* later in day	31	92	22	104	18	96·5
Phlegm*	None	61	117	61	117	138	97·5
	On waking *or* later in day	46	110	45	111	38	97
	On waking *and* later in day	36	93	26	108	11	90
Breathlessness	Grade 1 (none)	108	113	104	115	131	97·5
	,, 2	21	101	17	106	45	94
	,, 3 or more	14	97	11	109	11	96
Wheezing	None	49	114	48	116	84	98
	Occasional	73	110	68	113	88	97
	Most days/nights	21	97	16	112	14	88
Effects of weather on chest	None	74	117	74	117	110	99
	Affected without dyspnoea	31	110	30	112	36	94
	Affected with dyspnoea	38	95	28	108	41	95
Chest illnesses in past 3 years lasting more than 1 week	None	83	117	83	117	86	98
	One only	34	105	30	113	48	98
	Two or more	26	91	19	104	53	96
	One or more without increased phlegm	27	110	24	117	41	96
	One or more with increased phlegm	33	91	25	102	60	97

* Answers at second interview for men.

There is very little depression of M.B.C. in men with only occasional wheezing, with susceptibility to adverse weather which does not result in dyspnoea, with only one chest illness, or with any number of illnesses unassociated with increased phlegm production.

The women, on the other hand, show no significant reduction of M.B.C. in association with any of the symptoms.

Symptoms and Smoking Habits

It was shown in Table I that, of all the symptoms, only cough and sputum were significantly commoner in the men than in the women. This difference might be due to differences in smoking habits, for, as Table VIII shows, the men were heavier smokers than the women. The prevalence of cough and sputum increases significantly with increasing tobacco consumption in both sexes (Table IX). Among the heavier smokers (15 or more grammes of tobacco daily) there are no significant differences between the prevalences in the two sexes. Among the non-smokers and light smokers the prevalence of cough and phlegm is higher in the men than in the women, though the differences are only just significant. Of the non-smokers and light smokers, significantly more of the men than of the women had smoked heavily in the past; but among these former heavier smokers the prevalence of cough and phlegm

TABLE VIII.—*Number of Subjects with Different Smoking Habits*

Present Smoking Habits	Men			Women		
	Aged 40–49	Aged 50–59	All Ages	Aged 40–49	Aged 50–59	All Ages
Non-smokers	13	13	26	49	50	99
Never smoked	6	4	10	43	43	86
Smokers:						
1–14 g. a day	60	54	114	34	37	71
15–24 ,, ,,	20	22	42	9	7	16
Over 25 g. and more a day	3	7	10	4	2	6
Total	96	96	192	96	96	192

1 cigarette = 1 g. of tobacco.

was no greater than in those who had always been light smokers. The rather higher prevalence of cough in the younger compared with the older women does not appear to be due to differences in smoking habits; for the proportions of heavy, light, and non-smokers in the two age groups were almost identical (Table VIII).

Although the numbers of men who had never smoked was small, their mean M.B.C. is significantly higher than that of the ex-smokers or smokers (Table X). The differences between ex-smokers, lighter, and heavier smokers are not significant. One non-smoker had a history of bronchiectasis, and it was this man who was dyspnoeic and had had more than two recent chest illnesses. Apart from this man the non-smokers are almost asymptomatic (Table X). There are otherwise no significant differences in prevalence of symptoms in the different smoking groups in either sex, although dyspnoea grade 3, persistent wheezing (in women), and chest illnesses (in men) appear to be rather more frequent in the heavier smokers. Our findings are similar to those of Higgins (1959), but different from those of Oswald and Medvei (1955), who found a similar prevalence of bronchitis in male and female civil servants with similar smoking habits. The sex contrasts we have found may be associated with the differences of occupation between our men and women. The greater frequency of cough and phlegm in the men with the smaller tobacco consumption compared with the women might, for example, be due to their exposure on their rounds to London's polluted air.

Comparison With Other Surveys

Comparisons between the prevalence of respiratory symptoms that we observed and the prevalence reported by other authors are difficult because of the effects of technique and definitions. It would be most interesting to know whether our subjects had more or less "chronic bronchitis" than was found by Pemberton (1956) in rural, urban, and coal-mining populations in America. Pemberton defined chronic bronchitis as "chronic cough and sputum," but introduced other considerations in doubtful cases such as the occurrence of chest illnesses and whether or not colds went to the subjects' chests. He also excluded cough apparently due to smoking. The introduction of such qualifications to varying degrees precludes valid comparisons. Pemberton's findings in men aged 50–59 are shown in Table XI, and are compared with the prevalence of different levels of chronic cough and sputum in our cases. It is seen that, according to the definition of chronic bronchitis used,

TABLE XI.—*Comparison with Prevalence of Cough and Sputum Reported by Pemberton* (1956) *in Males in U.S.A. Aged* 50–59

Population	No.	Percentage with "Chronic Bronchitis"		
Pemberton (1956) (U.S.A.):				
Coal-workers	108	29		
Urban dwellers	68	15		
Rural ,,	110	12		
		Type 1*	Type 2†	Type 3‡
Present study:				
Postmen (London)	96	39	16·5	12·5

* Cough and sputum at least on rising in the winter.
† Cough and sputum throughout the day in the winter.
‡ Same + "colds usually go to the chest."

TABLE IX.—*Relationship Between Present Smoking Habits and Prevalence of Cough and Sputum*

Present Smoking Habits	No.		Percentage with							
			Cough in Winter				Phlegm in Winter			
			On Rising		All Day		On Rising		All Day	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
Non-smokers	26	99	27 (a)	9 (b)	11·5 (c)	3 (d)	23 (e)	15 (f)	15 (g)	1 (h)
1–14 g. a day	114	71	46 (i)	30 (k)	16 (l)	10 (m)	39 (n)	23 (o)	18 (p)	8·5 (q)
15 g. or more a day	52	22	64	73	23	32	44	45	19	13·5

Significant differences (χ^2)
a v b: P = 0·02–0·1.
g v h: P = 0·001.
i v k: P = 0·05–0·02.
n v o: P = 0·05–0·02.

Insignificant differences (χ^2)
c v d: P = 0·1–0·05.
e v f: P = 0·5–0·3.
l v m: P = 0·3–0·2.
p v q: P = 0·3–0·2.

TABLE X.—*Numbers of Subjects Admitting to Various Symptoms (percentages in brackets) and Mean Indirect M.B.C. (standardized to age* 40) *According to Smoking Habits*

Sex	Smoking Habits	No.	Dyspnoea		Wheezing Most Days or Nights	Dyspnoea in Adverse Weather	One or More Illnesses with Increased Phlegm	Two or More Illnesses with Increased Phlegm	Winter Catarrh	Mean Indirect M.B.C. (l./min.). (No. of Subjects in Brackets)
			Grade 2	Grade 3+						
Men	Never smoked	10	—	1 (10)	—	2 (20)	1 (10)	1 (10)	4 (40)	132·8 (8)
	Past smoker	16	3 (19)	1 (6)	2 (12·5)	4 (25)	3 (18·5)	1 (6)	6 (37)	106·1 (11)
	Smoker: 1–14 g. a day	114	17 (15)	8 (7)	19 (16·5)	28 (24·5)	20 (17·5)	13 (11·5)	46 (40)	110·9 (87)
	,, 15 g. or more	52	7 (13·5)	7 (13·5)	8 (15·5)	16 (31)	15 (29)	8 (15·5)	25 (48)	104·3 (37)
Women	Never smoked	86	23 (27)	4 (4·5)	2 (2·5)	17 (20)	28 (33)	14 (16·5)	25 (29)	99·3 (83)
	Past smoker	13	3 (23)	—	—	4 (31)	6 (46)	5 (38)	4 (31)	93·3 (13)
	Smoker: 1–14 g. a day	71	13 (18·5)	4 (5·5)	7 (10)	16 (22·5)	23 (33)	12 (17)	22 (31)	96·9 (70)
	,, 15 g. or more	22	7 (32)	3 (13·5)	5 (22·5)	5 (22·5)	5 (22·5)	2 (9)	11 (50)	96·1 (21)

Note.—The totals in each symptom group do not always tally with Table VII because of the inclusion of those who did not have their M.B.C. measured.

TABLE XII.—*Comparison Between Prevalence of Symptoms and Mean Indirect M.B.C. in Male and Female Post Office Workers aged 50–59 and Random Samples of Men and Women aged 55–64 Reported by Higgins* (1957) *and Higgins et al.* (1959).

Sex	Population	Age Group	No.	Percentage with							
				Cough and Sputum*	Breathlessness		Bronchitic Chest Illness†		"Chronic Bronchitis"‡	Mean Indirect M.B.C. (l./min.)	Mean Expiratory Peak Flow Rate (l./min.)
					Grade 2 and Over	Grade 3	Only One	More than One			
Male	Vale of Glamorgan ..	55–64	86	25·6	24·4	7·9	11·6	4·7	5·8	89	
	Leigh (Lancs) non-mining	55–64	84	17·9	22·6	7·2	4·8	13·1	10·7	85	
	Staveley (Derby) non-dusty	55–64	81	32·1	33·3	11·1	8·6	12·3	14·8	95	
	London postmen	50–59	96	29·2	34·4	14·6	6·3	14·6	15·7	91·4	
Female	Vale of Glamorgan ..	55–64	92	7·2	18·9	2·2	7·6	4·3	4·3		297
	London Post Office ..	50–59	192	11·5	29·8	6·3	11·5	15·7	11·4		325

* Positive to questions 1+6. † Positive to questions 43, 44, and 45. ‡ Positive to questions 6, 43, 44, 45 (at least one week's duration).

the prevalence in our subjects can appear greater than in Pemberton's coal-miners or the same as in his rural population. Comparisons are only justified between surveys in which the same questions have been asked. In the surveys reported by Higgins (1957) and Higgins *et al.* (1959) questions almost identical with some of ours were used.

Table XII shows a comparison between two non-mining groups of men aged 55–64 reported by Higgins and our male subjects aged 50–59. Our men were on the average five years younger than those studied by Higgins. Allowing for the decline of 1.2 l./min./year of age (which was the regression on age in our symptomless men) the mean M.B.C. of our men was almost exactly the same as that of the random sample of men in the town of Leigh, in Lancashire, but it was lower than that of the men in the town of Staveley or in the Vale of Glamorgan. The frequency of chest illnesses was much the same in all three urban groups but was lower in the rural men. Our men showed the highest prevalence of breathlessness, but the prevalence of cough and sputum was similar in all the areas except for a low figure in Leigh. For the women we can compare measurements of peak expiratory flow rate which Higgins made, using Wright's expiratory flow-meter (Wright and McKerrow, 1959), for we also used this instrument on our subjects. It will be seen that, again allowing for age, our figures are almost identical with his. All the symptoms, however, were more prevalent in our women than in his. In view of the similarity in the objective ventilatory function measurements the differences in symptom prevalence may be partly due to observer variation. The differences in cough and sputum are not accounted for by differences in smoking habits in the men; but our women were much heavier smokers than those in the Vale of Glamorgan, and this may well account for their having more cough and sputum. It is notable that the frequency of chest illnesses was similar in our men and in the urban men in Leigh, but both our men and our women had higher chest illness rates than their counterparts in the Vale of Glamorgan. This may be a true effect of urban residence.

Diagnosis of Chronic Bronchitis

Chronic bronchitis implies chronic inflammation of the bronchi of non-specific aetiology. It does not necessarily imply the presence of infection. The presence of inflammation cannot readily be established in life. The disease must in practice be defined and diagnosed upon the symptomatic consequences of the inflammation—namely, chronic cough and expectoration (when other causes of these symptoms have been excluded). Ever since Badham (1808) first introduced the word bronchitis to medical literature it has been customary to include dyspnoea together with cough and expectoration as an essential symptom of bronchitis. This custom has been supported recently in monographs on chronic bronchitis by Oswald (1958) and by Stuart-Harris and Hanley (1957). Oswald argues, "clearly there must be some disability to warrant a diagnosis of chronic bronchitis, otherwise anyone having occasional cough and sputum, possibly related to smoking, must be included." He refers to two types of disability—breathlessness and exacerbations of infection—the presence of either of which justifies the diagnosis. Stuart-Harris and Hanley admit that subjects with persistent cough and sputum but without dyspnoea may be in "the earliest phase" of chronic bronchitis, but prefer not to accept the diagnosis in the absence of breathlessness (which in an epidemiological study they found was highly correlated with recurrent illnesses), because to do so would result in a number of "healthy persons" being diagnosed as having bronchitis.

For the epidemiologist, concerned with aetiology, the "earliest phase" of bronchitis must be of special interest, since those subjects who are already disabled by the disease are beyond the reach of preventive medicine. It was for this reason that both Pemberton (1956) and Ogilvie and Newell (1957) accepted mere cough and sputum as evidence of bronchitis. There are pathological grounds for supposing that hypersecretion of mucus favours bronchiolar infection and that such recurrent infections may play an important part in the development of emphysema (Reid, 1954; Leopold and Gough, 1957; McLean, 1958).

For these reasons it seems to us logical from the point of view of pathogenesis, and essential from the point of view of preventive medicine, to admit to the diagnosis of bronchitis all those who have persistent cough and sputum. It seems to us as illogical to reject the diagnosis of bronchitis in those without associated disability as it would be to reject the diagnosis of hypertension in subjects with a raised blood pressure but without symptoms, or of chronic nephritis in the presence of persistent albuminuria but without uraemia. If this be accepted we must consider how to define chronic bronchitis. The first question is whether a productive cough indicating bronchial hypersecretion is essential, or whether a dry cough alone should be accepted.

Of the 144 men we studied on the second occasion, 12 (8.5%) admitted to cough but denied phlegm. All

but one of these men returned sputum bottles in one or other of the winter collections, and six of these 11 bottles contained sputum. A genuinely unproductive cough thus appeared to have been present in only five men. In these men it occurred only on rising in the morning, and all of them had indirect M.B.C.s at or above the mean of all the men without persistent sputum. In the women, 18 (9.5%) admitted to cough but denied phlegm. Fourteen of these women coughed on rising or later in the day, and only three produced specimens of sputum. None of them had a significant reduction of M.B.C. Thus, an unproductive cough persisting throughout the day was recorded in only four women, and in no case was it associated with impaired ventilatory capacity. Chest illnesses were no more frequent in these subjects than in those without cough or sputum. This conclusion will require confirmation on larger numbers of subjects, but meanwhile it seems reasonable to exclude from the diagnosis of chronic bronchitis subjects who do not produce sputum. There were nine men (6%) and 15 women (8%) who admitted to phlegm but denied cough. This inconsistency is not infrequent in clinical practice and may be attributed to the phlegm being produced without effort; for some people a cough implies a forceful action. Such cases should be included as having bronchitis.

We conclude that for our purposes, and within the framework of our questionary, *chronic bronchitis may be defined as "the production of phlegm on most days for at least three months in each year."* We may recognize two grades of chronic bronchitis as shown in Table II and Fig. 1. Grade 1 comprises those who produce phlegm only on rising or only later in the day, and grade 2 comprises those who produce phlegm both on rising and throughout the day.

These grades correspond approximately to those producing more or less than 2 ml. of sputum in the first hour after rising in the winter (Table IV). Those two methods of grading have similar degrees of repeatability (Table V), but the greater objectivity of measurement of sputum volume renders this the method of choice. Questions should also be asked because of their greater validity in relation to a chronic condition. In Great Britain chronic bronchitis is so much more prevalent than any other cause of chronic productive cough that it is not necessary to exclude other causes in epidemiological studies. For clinical purposes it is, of course, essential to do this before diagnosing chronic bronchitis.

Bronchitis with Disability

There are two chief kinds of disability in chronic bronchitis: recurrent chest illnesses and breathlessness. we have already discussed the validity and repeatability of questions concerning chest illnesses, and given our reasons for preferring to use measurements of the indirect M.B.C. to questions about breathlessness for estimating impairment of ventilatory function. We suggest the use of two grades of each of these forms of disability. For illnesses we distinguish, as does Higgins (1957), those with only one and those with two or more chest illnesses in the past three years lasting for at least one week and associated with an increase of phlegm production. We have used this criterion of increased phlegm during the illnesses for three reasons. Firstly, because such an increase is a clinical characteristic of exacerbations of bronchitis. Secondly, because the indirect M.B.C. was significantly reduced in those with such illnesses but not in those with illnesses unassociated with increased sputum (Table VII). Thirdly, because of 21 chest illnesses occurring in men without bronchitis, 11 (53%) were associated with increased phlegm, while in those with grade 1 bronchitis 13 out of 19 (69%), and in those with grade 2 bronchitis 20 out of 22 (91%), had this association.

We have used two grades of impaired ventilatory capacity, the first comprising those with a standardized indirect M.B.C. lying between one and two standard deviations below the mean of all subjects, excluding those with grade 2 bronchitis, and the second comprising those with a standardized indirect M.B.C. falling more than two standard deviations below this mean. These grades correspond to values of 60–80% and less than 60% of the expected figure for the subject's age. Table XIII shows the highly significant relationship between the grade of bronchitis and these two forms of disability in the men.

TABLE XIII.—*Relationship Between Grade of Bronchitis Based on Answers to Questions and Bronchitic Chest Illnesses and Impairment of Age-standardized Indirect M.B.C. Numbers of Men: Percentages in Brackets*

Symptomatic Grade of Bronchitis	Chest Illnesses			Indirect M.B.C.		
	None	Only One	2 or More	Higher than 1 S.D. Below Mean	1–2 S.D. Below Mean	More than 2 S.D. Below Mean
0	51 (82·5)	7 (11)	4 (6·5)	52 (86)	9 (15)	0
1	34 (74)	5 (11)	7 (15)	36 (78·5)	9 (19·5)	1 (2)
2	17 (47·5)	6 (16·5)	13 (36)	20 (56)	6 (16·5)	10 (27·5)
Total	102 (71)	18 (12·5)	24 (16·5)	108 (76)	24 (16·5)	11 (7·5)
	$\chi^2 = 17{\cdot}2$ $P < 0{\cdot}001$			$\chi^2 = 28{\cdot}5$ $P < 0{\cdot}001$		

We did not find that any other combinations of questions enabled us to discriminate more accurately between the grades of sputum volume, or between those with and without impaired M.B.C., than did the simple questions about phlegm and illnesses. There was, however, a significant association between bronchitis with disability (either from illnesses or from impaired ventilatory capacity) and the presence of dyspnoea, wheezing on most days and nights, and colds or adverse weather affecting the chest. We therefore suggest that questions on these symptoms should be retained in questionaries for the study of chronic respiratory disease, since important correlations or differences might emerge. For instance, the effect of weather on the chest in bronchitics might provide a useful contrast between subjects living in different areas with different levels of air pollution.

Bronchitis in Men and Women

Mortality from bronchitis in England and Wales is four times as great in men as in women of the ages with which we were concerned, and clinical experience reveals a similar sex difference in patients attending hospital (Oswald, 1958; Stuart-Harris and Hanley, 1958).

The picture of bronchitis that emerges from our study is different in the two sexes. Cough and sputum, but no other symptoms, were more prevalent in the men; all symptoms showed an age gradient in the men but not in the women, and a significant depression of ventilatory capacity in association with symptoms occurred only in the men. We have seen that

differences in smoking habits do not entirely account for the different prevalence of cough and sputum nor for the lack of age gradient in the women. It is possible that women with disability are less likely than men to stay in employment, so that occupational selection may have been partly responsible, although disability would be less likely to interfere with the sedentary work of the women than that of the men, and Higgins (1957) also found little or no age gradient in prevalence of "chronic bronchitis" (cough and sputum with chest illnesses) in women between the ages of 35 and 64. Exposure of our men to the polluted air of the City of London may be partly responsible for the sex differences that we observed, for Fairbairn and Reid (1958) have shown that postmen exposed to air pollution in their daily rounds have higher sickness absence rates from bronchitis than do civil servants working indoors, and that this difference increases with advancing age. However, the striking lack of impairment of ventilatory function in association with cough and sputum and recurrent chest illnesses in the women does suggest that bronchial hypersecretion and recurrent infection have rather different consequences in the two sexes, and that this difference may be at least partly responsible for the sex differences in disability and mortality from chronic bronchitis.

Summary

192 postmen and 192 female Post Office employees in London age 40–59 were studied by a symptomatic questionary, by measurements of sputum volume and of ventilatory capacity, and by inspection of sickness absence records.

The men had more cough and sputum than the women, but the prevalence of other symptoms and of chest illnesses was similar in the two sexes. Symptoms increased with age in the men but not in the women. These differences were only partly attributable to differences in smoking habits.

The severity of phlegm production was graded according to whether or not it occurred throughout the day, and this grading correlated well with the volume of sputum produced in the first hour after waking. Whether or not the phlegm was said to be perennial appeared not to matter. Ventilatory capacity was significantly impaired in the men, but not in the women, who had the higher grade of phlegm production, frequent wheezing, susceptibility to adverse weather, and a history of chest illnesses with an increase of phlegm production.

It is suggested that chronic bronchitis should be diagnosed in subjects with a productive cough not due to other causes, and that it should be graded in severity either according to the persistence of the symptom throughout the day or according to the volume of sputum expectorated. Disability from impairment of ventilatory capacity or recurrent chest illnesses should be regarded as complications, and not as essential features of chronic bronchitis, since it is important to recognize the disease before it has resulted in disability. Only prospective studies can determine the prognosis of the suggested grades of bronchitis in respect of the development of disability.

The disabling form of the disease can be referred to as "chronic bronchitis with ventilatory impairment" and "chronic bronchitis with recurrent exacerbations," and may be graded according to the severity of the impairment and the frequency of exacerbations. Disability appears to be a less frequent consequence of chronic bronchitis in men than in women.

We thank the Post Office authorities for permitting the investigation, their staff for much assistance, and the Union of Post Office Workers and the Civil Service Clerical Association for their support. We also thank the Health Committee of the London County Council for allowing three of their health visitors to take part in the study, and to Miss Axtens, Mrs. Rutter, and Miss Underwood for their careful work. We are particularly grateful to Dr. P. Hugh-Jones for his insistence that unless we collected sputum specimens he would mistrust our symptomatic inquiry. Finally, we thank all the subjects of our investigation for their ready co-operation. Dr. C. M. Fletcher was in receipt of a grant for expenses from the Medical Research Council.

Extract from Questionary Referred to in Text

Question No.

1. Do you usually have a cough? Yes/No

Do you cough at all when you get up or first thing in the morning:

2. (*a*) in the winter? Yes/No
3. (*b*) in the summer? Yes/No

Do you go on coughing during the day:

4. (*a*) in the winter? Yes/No
5. (*b*) in the summer? Yes/No
6. Do you usually bring up phlegm from your chest (not from back of your nose)? Yes/No

Do you bring up any phlegm at all when you get up first thing in the morning:

7. (*a*) in the winter? Yes/No
8. (*b*) in the summer? Yes/No

Do you bring it up during the day:

9. (*a*) in the winter? Yes/No
10. (*b*) in the summer? Yes/No

Is this phlegm:

11. (*a*) always clear white, grey, or blackish? ☐
12. (*b*) occasionally yellow or green, at least in parts? ☐
13. (*c*) usually yellow or green? ☐

How long have you had this morning cough/phlegm in the winter:

14. (*a*) less than one year? ☐
15. (*b*) one to three years? ☐
16. (*c*) more than three years? ☐
17. Breathlessness (average in last winter)

Grade 1. Are you ever troubled by breathlessness except on strenuous exertion? ☐

Grade 2. (If yes). Are you short of breath when hurrying on the level or walking up a slight hill? ☐

Grade 3. (If yes). Do you have to walk slower than most people on the level? Do you have to stop after a mile or so (or after ¼ hour) on the level at your own pace? ☐

Grade 4. (If yes to either). Do you have to stop for breath after walking about 100 yds. (or after a few minutes) on the level? ☐

Grade 5. (If yes). Are you too breathless to leave the house, or breathless after undressing? ☐

21. Does your breathing ever sound wheezy or whistling? Yes/No
22. If yes: (*a*) occasionally (for example, when you have a cold)? ☐
23. (*b*) most days (or nights)? ☐

When you have a cold in the head, does it go to your chest (i.e., is it followed by increased cough or phlegm):

28. (*a*) never or only occasionally? ☐
29. (*b*) usually or always? ☐

31.	Does the weather affect your chest ?	Yes/No
31a.	(If no, check " not even fog or cold ? ")	Yes/No
35.	Does it make you wheeze ?	Yes/No
38.	Does it make you breathless ?	Yes/No
	Apart from colds, do you usually have a stuffy nose or catarrh at the back of your nose ;	
41.	(*a*) in the winter ?	Yes/No
42.	(*b*) in the summer ?	Yes/No
43.	During the last three years have you had a chest illness which has kept you in bed, off work, or indoors ?	Yes/No
43a.	(If no, check " not even 'flu ? ")	Yes/No
	If yes to 43 or 43a :	
44.	(*a*) did you have increased cough with the illness(es) ?	Yes/No
45.	(*b*) did you have increased phlegm with the illness(es) ?	Yes/No
46.	(*c*) did you have only one such illness ?	☐
47.	(*d*) did you have more than one such illness ?	☐
48.	(*e*) estimated average duration	
62.	Do you smoke ?	Yes/No
63.	(If no) Have you ever smoked ? (Record " No " if less than 1 a day for a year)	Yes/No
	(If yes) :	
	Cigarettes a week	
	Ounces of tobacco/week (hand-rolled)	
	Ounces of tobacco/week (pipe)	

REFERENCES

Badham, C. (1808). *Observations on the Inflammatory Affections of the Mucous Membrane of the Bronchiae.* Callow, London.
Brit. med. J., 1959, **1**, 157.
Cochrane, A. L., Chapman, P. J., and Oldham, P. D. (1951). *Lancet*, **1**, 1007.
Elmes, P. C., Dutton, A. A. C., and Fletcher, C. M. (1959). Ibid. In press.
—— Fletcher, C. M., and Dutton, A. A. C. (1957). *Brit. med. J.*, **2**, 1272.
Fairbairn, A. S., and Reid, D. D. (1958). *Brit. J. prev. Soc. Med.*, **12**, 94.
—— Wood, C. H., and Fletcher, C. M. (1959). To be published.
Fletcher, C. M. (1952). *Proc. roy. Soc. Med.*, **45**, 577.
Gandevia, B., and Hugh-Jones, P. (1957). *Thorax*, **12**, 290.
Higgins, I. T. T. (1957). *Brit. med. J.*, **2**, 1198.
—— (1959). Ibid., **1**, 325.
—— Cochrane, A. L. Gilson, J. C. (1959). To be published.
—— Oldham, P. D., Cochrane, A. L., and Gilson, J. C. (1956). Ibid., **2**, 904.
Leopold, J. G., and Gough, J. (1957). *Thorax*, **12**, 219.
McLean, K. H. (1958). *Amer. J. Med.*, **25**, 62.
Ogilvie, A. G., and Newell, D. J. (1957). *Chronic Bronchitis in Newcastle-upon-Tyne.* Livingstone, Edinburgh.
Oswald, N. C. (1958). *Recent Trends in Chronic Bronchitis.* Lloyd-Luke, London.
—— and Medvei, V. C. (1955). *Lancet*, **2**, 843.
Pemberton, J (1956). *A.M.A. Arch. industr. Hlth*, **13**, 529.
Reid, L. McA. (1954). *Lancet*, **1**, 275.
Scadding, J. G. (1952). *Quart. J. Med.*, **21**, 460.
Stuart-Harris, C. H., and Hanley, T. (1957). *Chronic Bronchitis, Emphysema, and Cor Pulmonale.* Wright, Bristol.
Wright, B. M., and McKerrow, C. B. (1959). To be published.

Retirement is largely a twentieth-century problem, the size of which can be gauged by the estimate that there will be about 10 million people of pensionable age in this country by 1970. A study group appointed in 1955 by the National Old People's Welfare Council has recently issued an outline of the ways in which people can prepare themselves to meet the psychological and practical difficulties they will be faced with in their old age (*Preparation for Retirement or Adjustment to Ageing*, National Council for Social Service, price 1s. 6d.).

SECRETION OF BLOOD-GROUP SUBSTANCES IN RHEUMATIC FEVER

A GENETIC REQUIREMENT FOR SUSCEPTIBILITY ?

BY

A. A. GLYNN, M.B., M.R.C.P.

L. E. GLYNN, M.D., M.R.C.P.

AND

E. J. HOLBOROW, M.D.

Rheumatism Research Unit (Medical Research Council), Canadian Red Cross Memorial Hospital, Taplow, Maidenhead, Berkshire, England

In a previous study of rheumatic fever subjects we reported an unduly high incidence of non-secretors of ABH blood-group substances (Glynn *et al.*, 1956). This result was based mainly on findings with a single test in which the readily precipitable Le^a substance present in the saliva of most ABH non-secretors was detected by means of rabbit anti-Le^a precipitating serum. This test gave results in close agreement with red-cell Lewis phenotypes and was positive with most A, B, or AB salivas giving negative agglutination inhibition tests for A and B substances.

In the present work we have used this test and also the " ulex " test for secretion of ABH substances to estimate the frequencies of both ABH non-secretors and Le^a non-secretors in normal schoolchildren. In addition, a number of rheumatic fever cases have been added to the series, including 79 salivas from rheumatic fever cases in New York State, kindly made available for test by Dr. Harrison Wood, Medical Director, Irvington House, Irvington-on-Hudson, N.Y.

Many rheumatic fever salivas previously tested only for Le^a precipitation have now been retested for inhibition of ulex extract (see below).

Materials and Methods

1. Fresh specimens of saliva were obtained from approximately equal numbers of schoolchildren of each sex in the area of Slough, Bucks, whose ages were evenly distributed between 5 and 15 years. Specimens were collected, boiled for 10 minutes within two hours of taking, and stored at 4° C. until tested.

2. *Tests for ABH and Le^a Substances in Saliva.*—(*a*) ABH secretors were detected by testing saliva for its ability to inhibit the natural agglutinins (lectins) for human group O cells present in extracts of gorse seed (*Ulex europaeus*). The method is described by Boyd and Shapleigh (1954). (*b*) Le^a substance in the saliva was detected, using rabbit anti-Le^a precipitating serum as previously described. Positive results were obtained only with salivas negative in the gorse-extract test.

Results

Secretor and Lewis Gene Frequencies in Normal Schoolchildren

Table I shows the results of testing 669 healthy children's salivas with ulex extract and with rabbit-anti-Le^a serum. Le^a substance was detected by precipitation in 21% of these, and H substance by

TABLE I.—*Saliva Phenotypes in 669 Healthy Schoolchildren*

Reagent	Substance Detected	Positive	
		No.	%
Ulex extract	H	516	77·1
Rabbit anti-Le^a (precipitation) serum ..	Le^a*	139	20·8
Both H and Le^a absent		14	2·1

* Detected in non-secretors of H only.

inhibition in 77%, these two categories being mutually exclusive. In 2% neither test was positive.

The ulex results give the frequency of H non-secretors as 153/669=0.2287. These are individuals homozygous for the recessive secretor gene *se*, and the frequencies of the secretor alleles may therefore be calculated:

$$\left.\begin{array}{l} se=\sqrt{0.2287}=0.4783 \\ Se=\ 1-0.4783=0.5217 \end{array}\right\} \text{S.E.}=0.019$$

The genotype frequencies, therefore, are:

$$\left.\begin{array}{l} SeSe=0.2722 \\ Sese=0.4990 \end{array}\right\} \text{Secretors (0.7712)}$$

$$sese=0.2287 \quad \text{Non-secretors}$$

$$\text{Total } 0.9999$$

Table I also gives information about the Lewis gene frequencies. Thus among the total of 153 (ulex-negative) non-secretors 14 showed no precipitable Le^a substance in their salivas. It has previously been shown (Glynn *et al.*, 1956; Brown *et al.*, 1959) that when Le^a substance is present in non-secretors' saliva it is always in precipitable form. We may therefore assume that Le^a substance is absent from the salivas of these 14 non-secretors. Since, according to Ceppelini (1955), the Lewis (*L,l*) genes and the secretor genes segregate independently, the proportion 14/153 obtained from observation of the non-secretors provides an estimate of the frequency of the genotype *ll* in the whole population. The Lewis gene frequencies are thus obtainable:

$$\left.\begin{array}{l} ll=14/153=0\,0915 \\ l=\sqrt{0.0915}=0\,3025 \\ L=1-0.3025=0.6975 \end{array}\right\} \text{S.E.}=0.037$$

The genotype frequencies are:

$$ll=0\,0915$$

$$Ll=0.4220$$

$$LL=0.4865$$

$$\text{Total } 1.0000$$

From these results we have calculated the frequencies of the various combined Lewis and secretor genotypes, which are set out in Table II.

TABLE II.—*Frequencies of Lewis and Secretor (ABH) Genotypes and Phenotypes in 669 Slough Schoolchildren. (Based on Ulex and Le^a Precipitation Results Only)*

Frequency	Genotype	Saliva Phenotype			Red Cell Phenotype
		H	Le^a	Le^b	
0·1319	*SeSe LL*	+	(+)	+	Le(a−b+) 0·6996
0·1144	*SeSe Ll*	+	(+)	+	
0·2428	*Sese LL*	+	(+)	+	
0·2105	*Sese Ll*	+	(+)	+	
0·1113	*sese LL*	0	+	0	Le(a+b−) 0·2078
0·0965	*sese Ll*	0	+	0	
0·0248	*SeSe ll*	+	0	0	Le(a−b−) 0·0931
0·0456	*Sese ll*	+	0	0	
0·0227	*sese ll*	0	0	0	

Se=Secretor gene for ABH substance. *se*=Non-secretor gene for ABH substance. *Ll*=Allelomorphic genes for Le^a substance in saliva. +=Present 0=Absent. (+)=Not detectable with anti-Le^a (precipitation), but only by agglutination-inhibition.

Secretor Frequency in Rheumatic Fever

The present study adds 174 British and 79 American rheumatic fever cases to the 450 cases already reported by us. The majority of these have now been tested by both ulex and precipitation tests, but in 73 cases it has not been possible to do both tests, and in 11 the secretor status was determined exclusively by inhibition of anti-A and/or anti-B grouping sera. The methods of testing and results of the whole series are set out in Table III.

The simplest analysis of these figures is into secretor and non-secretor frequencies, including as secretors all

TABLE III.—*Salivary Tests in 703 Rheumatic Fever Cases*

Le^a Precipitin Test	Secretion Test	No.	Secretor Status
		British Cases	
Le^a−	H+	385	*Secretors* (ABH present in saliva)
Le^a−	A,B+	5	
Le^a n.d.	H+	8	
Le^a−	H n.d.	44	Mostly *secretors*, but includes one or two non-secretors of genotype *ll*
Le^a+	H−	146	*Non-secretors* (Precipitable Le^a present and/or ABH not detected)
Le^a+	A,B, −	6	
Le^a+	H n.d.	16	
Le^a n.d.	H−	5	
Le^a−	H−	9	
		American Cases	
Le^a−	H+	56	Secretor
Le^a+	H−	22	Non-secretor
Le^a−	H−	1	Non-secretor
	Total	703	

Le^a+=Precipitable Lewis^a in saliva. Le^a−=No precipitable Lewis^a in saliva. H+=H detected by ulex test. H−=H not detected by ulex test A,B+=A, B, or AB detected by agglutination inhibition test. A,B−=A, B, or AB *not* detected by agglutination inhibition test. n.d.=Test not done.

TABLE IV.—*Comparison of Rheumatic Fever Cases and Normal Schoolchildren. Saliva Tested with Ulex Extract*

Saliva	H+	H−	Total	% H−
Rheumatic fever	393	160	553	28·9
Healthy schoolchildren ..	516	153	669	22·9

$\chi^2=5.9$. n=1. P=<0·02.

TABLE V.—*Comparison of Rheumatic Fever Cases and Normal Schoolchildren. Saliva Tested with anti-Le^a (Precipitation)*

Saliva	Le^a−	Le^a+	Total	%Le^a+
Rheumatic fever	443	168	611	27·5
Healthy schoolchildren ..	890	239	1,129	21·2

$\chi^2=8.8$. n=1. P=<0·01.

of the 44 Le^a precipitin-negative subjects not tested for H. The whole series, British and American, gives 205 non-secretors, out of a grand total of 703 cases. This is a percentage of 29.16.

For the purposes of strict comparison with normal children, the results to be compared are those in which the same test has been carried out in both control and rheumatic fever cases. Considering the results of ulex testing, for example, we have a total of 553 British rheumatic children tested in this way and 669 normal children. The comparison of results in the two groups is set out in Table IV. The percentage of non-secretors in the rheumatic fever group is 28.9%, compared with 22.9% in the control group. This difference is significant at the 2% level ($\chi^2=5.9$; n=1; P=0.02–0.01).

A second comparison with an independent test—Le^a precipitation—is shown in Table V. Here the total number in the control group is much larger, and is composed of the 460 children originally tested and the

669 children reported above (total 1,129 normal children). The comparison of this large control group with the 611 British rheumatic fever cases which we have now tested with the anti-Le^a precipitating serum shows a highly significant difference ($\chi^2=8.8$; $n=1$; $P<0.01$). The American cases have not been included in either of these comparisons, as no normal control cases were available, but it is of interest that by both tests they give results closely similar to the British cases.

Discussion

In view of Ceppelini's (1955) demonstration that there is no correlation between the presence of Le^a substance and ABH substances in the saliva, the use of our Le^a precipitin test as an indicator of ABH secretor status may appear questionable. We have already shown, however (Glynn *et al.*, 1956), that the saliva precipitation test with rabbit anti-Le^a serum detects, under standard conditions, only Le^a secretors who are also non-secretors of ABH substances, and in the present work the good negative correlation with the ulex test confirms this. In the majority of Le^a secretors—that is, those who are also ABH secretors—Le^a substance is secreted in the saliva in a form detectable by agglutination inhibition tests, as used by Ceppelini, but not by precipitation. Although we have recently shown (Brown *et al.*, 1959) that the Le^a substance in the saliva of ABH secretors differs qualitatively (as well as quantitatively) from that of ABH non-secretors, it nevertheless remains true that if, as Ceppelini claims, Le^a and ABH secretion segregate independently, there should be the same proportion of Le^a non-secretors among ABH secretors as among ABH non-secretors. It is on this basis that the Lewis genotype frequencies have been calculated in Table II.

Our findings, then, may be discussed under two headings: the distribution of Lewis and secretor genotypes among normal children, and the deviation from this distribution found in a series of rheumatic fever cases.

Lewis and Secretor Genotypes in Normal Children

In using results of Le^a precipitin tests on saliva to estimate ABH non-secretor frequencies allowance must be made for ABH non-secretors who are also non-secretors of Le^a substance. Our previous series (Glynn *et al.*, 1956) contained 25 A, B, or AB non-secretors (whose saliva had been tested for inhibition of anti-A and anti-B agglutinating sera); of these, 23 gave positive Le^a precipitation tests, so that 2 out of 25 were non-secretors of precipitable Le^a substance. This figure was combined with those reported by Grubb and Morgan (1949) and by Race *et al.* (1949)—totalling 3 out of 108—to give 5 out of 133 (3.75%) as an estimate of the frequency of Le^a non-secretors among ABH non-secretors. That this was an underestimate is suggested both by Ceppelini's work in Italy, which revealed an incidence of non-secretors of Le^a substance of nearly 12%, and by our own figure of 9%, reported above, for British children.

Lewis and Secretor Genotypes in Rheumatic Fever

In view of the large number of cases and controls in this study, the results leave little doubt that a significant difference exists between the incidence of non-secretion of ABH substances in patients with rheumatic fever and in a corresponding group of normal subjects. Although significant, the observed difference of 6 to 7% would not appear at first sight to be of aetiological importance. However, from the calculated frequency of the secretor genes *Se* and *se* in the normal population it may be seen that if the gene *se* were essential for the development of rheumatic fever the expected incidence of non-secretors in a population with rheumatic fever would be 31.4%, which is not significantly different on these numbers from the observed figure of 29.1%. Thus if the gene *se* is essential for the development of rheumatic fever, then subjects with this disease must be either *Sese* or *sese*, and the frequency of non-secretors—that is, individuals of genotype *sese* in such a population—would be:

$$\frac{sese}{Sese+sese} = \frac{0.2287}{0.4990+0.2287} = 0.314 = 31.4\%$$

We therefore provisionally advance the hypothesis that rheumatic fever can develop only in individuals of genetic constitution *Sese* or *sese*. Since it is at present impossible to distinguish homozygous secretors, *SeSe*, from heterozygous secretors, *Sese*, confirmation of this hypothesis is obtainable only from some form of family study. If, for example, families are chosen in which one parent has rheumatic fever and is a secretor whilst the spouse is a non-secretor, then evidence of the genetic constitution (presumptive heterozygote) of the propositus with regard to secretion may be obtained from a study of the secretor status of the offspring. Thus the incidence of non-secretors amongst the children would be approximately 50% if the hypothesis were true and approximately 33% if false, since heterozygous secretors in the normal population are about twice as common as homozygous secretors (see Appendix I). Alternatively, the recognition of a few such families with eight or more children, all of whom were secretors, would go far to disprove the hypothesis.

If, as is postulated, all cases of rheumatic fever carry the non-secretor gene *se*, then compared with a normal population there will be an increased number of carriers of *se* in the parents and sibs of such cases. This increased frequency should be a measure of the increased liability, on purely hereditary grounds, of the parents and sibs to develop rheumatic fever.

The increased frequency of *se* carriers expected has been calculated (see Appendix II) to be 1.13/1 in the parents and 1.16/1 in the sibs of rheumatic fever patients.

The observed frequencies of rheumatic fever compared with a normal population are: parents 1.44/1, sibs 1.64/1. These figures are based on Taplow records. Similar ratios calculated from the literature vary from 4 (Read *et al.*, 1938) to 30 (Uchida, 1953).

There are several possible explanations for the excess incidence of rheumatic fever found as compared with that expected, the most likely being that the excess is due to patients and their families both being exposed to environmental conditions favourable to the development of rheumatic fever. Indeed, it has been argued that environmental factors could account for the whole of the supposed familial tendencies of rheumatic fever (Griffith *et al.*, 1948).

Secondly, there may be a further hereditary mechanism so far undiscovered. In view of the complicated interaction of secretor and Lewis genes already known, the possibility of further modifying genes cannot be excluded.

From the calculations in Appendix II the increased incidence of rheumatic fever expected in the parents of

patients with this disease would, on this hypothesis, be only some 13% and in the sibs some 16%. In view of the undoubted importance of environmental factors such small genetic factors would be almost entirely obscured except in impracticably large series. Failure, therefore, to establish a significant role for genetic factors in any ordinary series of cases in no way invalidates the present hypothesis.

Although it has been postulated that rheumatic fever is related to the presence of the non-secretor gene, one would not expect a parallel variation in different populations. The incidence of rheumatic fever varies enormously with local factors, particularly with those affecting the spread of streptococci. For instance, 38% of North American Negroes are non-secretors (Mourant, 1954), the gene frequency of *se* being 0.62, but the incidence of rheumatic fever is variously reported as equal to or higher or lower than that in the white population (Friedberg, 1950). Non-secretors are extremely rare among North American Indians, forming only 1.5% of the Navajos (Boyd and Boyd, 1949). Even fewer have been reported in other tribes: 0/79 in the Utes (Matson and Piper, 1947) and 1/210 in the Blood Indians (Chown and Lewis, 1953). Even so, this means that in the Navajos, for example, the gene frequency of *se* is 12%, and that 22% of the population carry the *se* gene in double or single dose.

Moreover, a study of hospital admission rates (Navajos) (Salsbury, 1937), comparative mortality rates (Navajos) (Smith, 1957), and rejections (all tribes) on cardiovascular grounds by selective service boards (McGibony, 1942) suggests that rheumatic heart disease may be less common among Indians than among the rest of the U.S. population. However, in Indians, as in others, environment is the overriding factor, and Paul and Dixon (1937), in a survey of Indian schoolchildren in three different areas, give the incidence of rheumatic heart disease as 4.5% in the north (Crows, Shoshones, and Arapahoes), 1.9% in the middle (Navajos), and 0.5% in the south (Pimas and Papagos). The 4.5%, which is unusually high for any population, is explained by the long Montana winters coupled with a degree of overcrowding not usually reached even in the slums of New York. (Three generations per room is usual.)

Finally, it is very dangerous to compare two groups so different in genetic make-up and in environment as Southern English schoolchildren and North American Indians. What would be most useful would be to know the genotypes of individual Indians with undoubted rheumatic fever.

APPENDIX I

If the above hypothesis be true, then all the secretor rheumatic fever subjects are of genotype *Sese*, and if these were mated with non-secretor individuals of genotype *sese* the incidence of non-secretors amongst the offspring would be 50%.

If the hypothesis be false, then there is no reason to expect that the ratio of heterozygote to homozygote secretors in rheumatic fever would differ from that in the normal population—that is, approximately 2 to 1. In those families in which the propositus is homozygous (*SeSe*) and the spouse *sese* all the offspring would be secretors. In those families in which the propositus is heterozygous (*Sese*) and the spouse *sese* 50% of the offspring would be secretors and 50% non-secretors. Since this second type of family would be approximately twice as common as the former, the incidence of non-secretor children in a randomly chosen group of such families would be 33%.

APPENDIX II

Calculation of the Frequency of Carriers of *se* in the Families of Rheumatic Fever Patients

Phenotypes	*Genotypes*	*Genotype frequency* (based on Slough figures)	
Sec.	*SeSe*	0·2722	0·7712
	Sese	0·4990	
Non-sec.	*sese*	0·2287	

PARENTS

In a normal population there are three possible types of mating:

	Phenotypes	*Frequencies*		
1.	Sec. × sec.	$(0·7712)^2$	= 0·595	1·001
2.	Sec. × non-sec.	$2(0·7712 \times 0·2287)$	= 0·354	
3.	Non-sec. × non-sec. ..	$(0·2287)^2$	= 0·052	

1. The sec. × sec. matings are of three kinds:

	Genotypes	*Frequencies*		
a.	*SeSe* × *SeSe*	$(0·2722)^2$	= 0·074	0·595
b.	*SeSe* × *Sese*	$2(0·2722 \times 0·4990)$	= 0·272	
c.	*Sese* × *Sese*	$(0·4990)^2$	= 0·249	

Type a can never produce children carrying *se*, and therefore, *ex hypothesi*, will not occur among the parents of rheumatic fever patients. Type b:—Only half of the children of this type of mating will carry *se*, so that in the parents of a large population selected for *se*—for example, rheumatic fever patients—one would expect only half the normal frequency of this type of mating = 0.136. Type c:—Three-quarters of the children will carry *se*, and, similarly, one expects the frequency of this type of mating to be 3/4 (0.249) = 0.187.

2. The secretor × non-secretor type of mating is of two kinds:

	Genotypes	*Frequencies*		
d.	*SeSe* × *sese* ..	$2(0·2722 \times 0·2287) = 0·125$		0·354
e.	*Sese* × *sese*	$2(0·4990 \times 0·2287) = 0·229$		

All the children of both types will carry *se*, so that the expected frequencies of these matings are unchanged.

3. The non-secretor × non-secretor mating is of one type only, and all the children will be non-secretors. This mating also will have an unchanged frequency.

Mating Type	Frequency in Normal Population	Expected Frequency in Normal Population of Matings Genetically Capable of Yielding Offspring with *se*	Expected Frequency in Parents of R.F. Population
a. *SeSe* × *SeSe* ..	0·074	0·0	0
b. *SeSe* × *Sese* ..	0·272	0·136	0·187
c. *Sese* × *Sese* ..	0·249	0·187	0·257
d. *SeSe* × *sese* ..	0·125	0·125	0·171
e. *Sese* × *sese* ..	0·229	0·229	0·314
f. *sese* × *sese* ..	0·052	0·052	0·071
	1·001	0·729	1·000

For mating types c, e, and f, both parents carry *se*, so that the frequency of *se* carriers = frequency of mating type. In types b and d, only one parent carries *se*, so that the frequency of *se* carriers = half frequency of mating type. Hence frequency of *se* carriers in parent population = sum of mating frequencies c, e, and f + ½(b + d)/a+b+c+d+e +f = 0.598/0.729 = 0.82.

In a normal population there are 0.728 *se* carriers, so that the relative increase in parents of rheumatic fever patients is 0.82/0.728 = 1.13.

SIBS

Mating Type	Frequency in Parents of R.F. Patients	Proportion of Children Carrying *se*	Expected Frequency of Children Carrying *se*
a. *SeSe* × *SeSe* ..	0	0	0
b. *SeSe* × *Sese* ..	0·187	0·5	0·093
c. *Sese* × *Sese* ..	0·257	0·75	0·192
d. *SeSe* × *sese* ..	0·171	1	0·171
e. *Sese* × *sese* ..	0·314	1	0·314
f. *sese* × *sese* ..	0·071	1	0·071

∴ increased frequency of *se* carriers compared with a normal population is 0·841 0·728 = 1·16. This assumes that all types of mating have the same average family size.

Summary

The presence of the ABH and Le^a blood-group substances in the saliva of healthy schoolchildren and of cases of rheumatic fever has been studied. By the ulex test 22.9% of 669 healthy schoolchildren were non-secretors; the comparable figure for 553 rheumatic fever cases was 28.9%. Positive results with a precipitation test on the saliva with a rabbit anti-Le^a serum were obtained in 21.2% of 1,129 healthy schoolchildren and in 27.5% of 611 cases of rheumatic fever. These two differences, significant at the 2% and 1% level respectively, would be expected if rheumatic fever could develop only in those individuals who are homozygous or heterozygous for the non-secretor gene. On the basis of this hypothesis we have shown that the incidence of rheumatic fever in the parents and sibs of patients with this disease should not, on hereditary grounds, be more than 13 and 16% greater respectively than in the general population.

REFERENCES

Boyd, W. C., and Boyd, L. G. (1949). *Amer. J. phys. Anthrop.*, **7**, 569.
—— and Shapleigh, E. (1954). *Blood*, **9**, 1195.
Brown, P. C., Glynn, L. E., and Holborow, E. J. (1959). *Vox Sang. (Basel)*. In press.
Ceppellini, R. (1955). *5th Int. Congr. Blood Trans. Paris, 1954: Reports and Communications*, p. 207.
Chown, B., and Lewis, M. (1953). *Amer. J. phys. Anthrop.*, **11**, 369.
Friedberg, C. K. (1950). *Med. Clin. N. Amer.*, **34**, 609.
Glynn, A. A., Glynn, L. E., and Holborow, E. J. (1956). *Lancet*, **2**, 759.
Griffith, G. C., Moore, F. J., McGinn, S., and Cosby, R. S. (1948). *Amer. Heart J.*, **35**, 438.
Grubb, R., and Morgan, W. T. J. (1949). *Brit. J. exp. Path.*, **30**, 198.
McGibony, J. R. (1942). *Publ. Hlth Rep. (Wash.)*, **57**, 1.
Matson, G. A., and Piper, C. L. (1947). *Amer. J. phys. Anthrop.*, **5**, 357.
Mourant, A. E. (1954). *The Distribution of the Human Blood Groups*. Blackwell, Oxford.
Paul, J. R., and Dixon, G. L. (1937). *J. Amer. med. Ass.*, **108**, 2096.
Race, R. R., Sanger, Ruth, Lawler, Sylvia D., Bertinshaw, Doreen (1949). *Brit. J. exp. Path.*, **30**, 73.
Read, F. E. M., Ciocco, A., and Taussig, H. B. (1938). *Amer. J. Hyg.*, **27**, 729.
Salsbury, C. G. (1937). *Sthwest. Med.*, **21**, 230.
Smith, R. L. (1957). *Publ. Hlth Rep. (Wash.)*, **72**, 33.
Uchida, I. A. (1953). *Amer. J. hum. Genet.*, **5**, 61.

The *Manual of Nutrition*, first published in 1945, was originally the work of Dr. Magnus Pyke, who was at that time a member of the Scientific Adviser's Division of the Ministry of Food. Since 1945 the rapid advance in nutritional knowledge has necessitated considerable revision of the text and tables, and the present edition, the fifth, has been prepared by present members of the Scientific Adviser's Division (Food) of the Ministry of Agriculture, Fisheries and Food in consultation with Dr. W. T. C. Berry of the Ministry of Health.

It differs substantially from the previous edition; Part I has been considerably amended to take into account the prevailing climate of opinion on the fundamental aspects of nutrition; the section on digestion in Part III has been rearranged so that the subject can be more easily explained; an expanded section has been included in Part IV on the effect of cooking on foods and nutrients, because the information is not readily available from textbooks in general use. . . . The *Manual* was originally designed to meet the needs of the caterer—for use in teaching the principles of nutrition to people already possessed of practical knowledge of cooking and catering; but its range of usefulness has been extended to teachers of domestic science and their students and pupils, and to all who are in any way concerned with public health. It has been found valuable by many of these, and by others who realize that an understanding of the scientific basis of good feeding should be part of the everyday knowledge of an educated community (*Manual of Nutrition*, H.M.S.O., 3s. net).

ANTERIOR TIBIAL SYNDROME DUE TO ARTERIAL EMBOLISM AND THROMBOSIS

ISCHAEMIC NECROSIS OF THE ANTERIOR CRURAL MUSCLES

BY

BERNARD J. FREEDMAN, M.B., M.R.C.P.
Consultant Physician, Dulwich Hospital, London,

AND

C. H. R. KNOWLES, M.D.
Consultant Pathologist, St. Richard's Hospital, Chichester

The anterior tibial syndrome comprises the following clinical features. There is sudden onset of severe pain in the muscles of the anterior tibial compartment. They become swollen, hard, acutely tender to pressure and to stretching, and paralysed, with resultant foot-drop. The tibialis anterior always undergoes ischaemic necrosis; the extensor hallucis longus and extensor digitorum longus usually do so. After some hours a reddish-purple discoloration, bearing some resemblance to a bruise, appears in the skin overlying the muscle bellies. The peronei, which lie outside the compartment, are not affected. Pulsation in the dorsalis pedis artery ceases for a few days or longer. A neuropathy, evidently ischaemic, of the anterior tibial nerve causes paralysis of the extensor digitorum brevis and cutaneous anaesthesia of the first interdigital cleft. During the ensuing 7 to 21 days pain and tenderness in the affected muscles subside. Movement may return to those muscle fibres in which paralysis is due to neuropathy, and to those necrotic fibres in which regeneration takes place. Paralysis may persist indefinitely; the muscles then remain indurated and undergo fibrous replacement. Histologically the affected muscle shows the changes of ischaemic necrosis (Griffiths, 1940). Much of the necrotic muscle is ingested by macrophages and undergoes replacement fibrosis.

Cases fall into three categories:

1. *Unaccustomed exertion involving the anterior tibial muscle group.*—The onset occurs a few hours later. Sixteen cases, all in healthy young men, have hitherto been reported in detail: Vogt (1943); Sirbu *et al.* (1944), one case with bilateral involvement; Horn (1945), two cases; Tillotson and Coventry (1950); and Freedman (1954)—all after marching; Phalen (1948), one case after a half-mile walk; Pearson *et al.* (1948), one case with bilateral involvement after long-jumping on a hard surface; Hughes (1948), two cases after playing football; and Carter *et al.* (1949), six cases after football and one case after marching.

2. *Local exogenous mechanical factors causing a rise in intracompartmental pressure.*—Sirbu *et al.* (1944) describe the occurrence of the syndrome after repair of a small muscle hernia. Carter *et al.* (1949) describe two cases apparently due to blood from a transfusion tracking extravenously into the compartment.

3. *Embolic or thrombotic occlusion of the anterior tibial artery or parent trunk.*—Hughes (1948) describes a case occurring in a young man with polyarteritis nodosa, and Watson (1955) two cases, the first (embolic) occurring in a woman aged 51, with mitral stenosis,

aortic valve incompetence, and auricular fibrillation, and the second (described as embolic, but possibly thrombotic) in a woman aged 70 with hypertension, auricular fibrillation, and peripheral arteriosclerosis.

As the syndrome is uncommon, it was thought desirable to introduce this paper with a summary of the main clinical features. Five cases are reported—two due to embolism and three to thrombosis.

Case 1

On March 22, 1950, a housewife aged 63 experienced severe pain and loss of power which came on rather suddenly in the right leg, with some numbness in the right foot. This was followed a few minutes later by mild transient pain in the left leg. On examination two days later the tibialis anterior muscle and the long extensor muscles of the right leg were swollen and hard, excruciatingly tender to pressure and stretching, and completely paralysed, with consequent foot-drop. The overlying skin was purplish red. The patient lay supine with her affected limb flexed at hip and knee. In this position foot-drop was prevented by pressure of the sole on the couch. Attempts to straighten her knee and lower it to the couch caused intense exacerbation of the pain; this was due to consequent foot-drop and stretching of the affected muscles. Pulsation was absent from the right dorsalis pedis artery and present in the other arteries of both lower limbs. The skin of the feet and toes was normal in colour and temperature. Cutaneous sensibility was impaired in the first interdigital cleft. No inflamed veins were seen or felt, and there was no oedema.

Signs of mitral stenosis, cardiac enlargement, and auricular fibrillation were present; the ventricular rate was 74 and the blood pressure 160/95. There was no cardiac failure, nor was there evidence of disease elsewhere.

By the sixth day, when we were able to admit her, the pain had somewhat abated, but the discoloration, induration, paralysis, and hypaesthesia were unchanged. Faint pulsation was discernible in the right dorsalis pedis artery, and a day later it was of normal strength. On the 11th day Mr. A. N. McCrea performed decompression by means of an incision 10 in. (25 cm.) long into the deep fascia overlying the swollen muscles, but they bulged only slightly. Three biopsy specimens were taken. The superficial fibres were normal in colour, but the deeper ones were buff-coloured and avascular. Twenty-one days after the onset a very faint trace of voluntary contraction was detectable in the tibialis anterior and extensor hallucis longus. She was apyrexial throughout the acute stage.

Electrical Reactions (35th day).—Faradism—no response in the tibialis anterior, extensor digitorum longus, extensor hallucis longus, and extensor digitorum brevis; normal response in the peroneus longus and peroneus brevis. Interrupted galvanism—all these muscles responded. Pain, tenderness, and discoloration were now absent, though induration persisted.

By the 45th day dorsiflexion of the ankle and toes was present, though it was very weak. The patient was treated with interrupted galvanism and faradism, and a plaster back-splint was applied to minimize foot-drop. By the 60th day fairly strong dorsiflexion of the ankle and toes was possible, and contraction and relaxation of the muscles could be seen and felt, except for the medial half of the tibialis anterior, which remained indurated and functionless. A few days later she started to walk. Electrical tests on the 64th day showed response to faradism in all the muscles in which it had been previously absent; response to interrupted galvanism was likewise present. When seen again at the eighth month she reported that she was able to carry out ordinary household duties. All the previously affected muscles were found to contract firmly, except for the medial half of the tibialis anterior, which was still indurated. Cutaneous sensibility was still impaired in the first interdigital cleft.

In December, 1950, she developed a left hemiplegia, attributable to a cerebral embolism, from which she made a fairly good functional recovery.

Fourteen months after the onset a second biopsy of the tibialis anterior muscle was performed. The superficial part was pale greyish pink. It did not bleed or contract on incision except for the deeper fibres of the medial portion, which appeared normal.

Histological Findings

First biopsy, 11 days after the onset.—The material consisted of three small fragments of necrotic muscle. In two of the fragments the muscle fibres retained their normal size and shape, although most of the nuclei had disappeared (Fig. 1). A section stained by Mallory's phosphotungstic acid haematoxylin showed the transverse striae to be normal in a few fibres, while in others they were obscured or replaced by a diffuse granularity. Many fibres showed accentuation and widening of the transverse markings, Hensen's lines being clearly visible, and this change was seen to progress to transverse fragmentation with separation of the sarcomeres. A few fibres had begun to split longitudinally into separate myofibrils. Between the fibres there were thin deposits of finely granular basophilic debris, sparsely infiltrated by polymorphonuclear leucocytes. In many areas of the third fragment the dead fibres were undergoing invasion and phagocytosis by macrophages, a few of which had two or more nuclei; fibroblasts were also present in small numbers, but there was no collagenous fibrosis. All stages could be found between fibres of normal size which had retained their structural outlines and contracted endomysial sheaths within

FIG. 1.—Case 1. Necrotic muscle in longitudinal section, showing accentuation of transverse markings, early fragmentation, and disappearance of nuclei. A collection of extravasated erythrocytes is shown in the interstitial tissue. (Haematoxylin and eosin ×110.)

which recognizable muscle substance had been completely replaced by swollen macrophages (Fig. 2). A reticulin impregnation showed that, as the muscle substance disappeared, the endomysial framework shrank *pari passu* but remained essentially intact. The arterioles appeared contracted but structurally normal. Capillary engorgement and extravasation of erythrocytes were seen in many areas, but the latter was possibly an operative artifact. Traces of free iron were found, mostly within necrotic muscle fibres. No evidence of regeneration of muscle was seen. The appearances were those of acute ischaemic necrosis of recent origin.

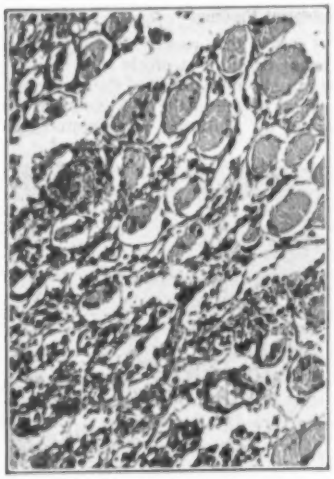


FIG. 2.—Necrotic muscle in transverse section, showing phagocytosis of dead fibres. (H. and E. ×110.)

Second biopsy, 14 months after the onset.—The excised fragments of muscle showed moderate diffuse collagenous thickening of the endomysial and perimysial connective tissue. As a result the architectural pattern was slightly irregular, but the appearance of the muscle fibres themselves was within normal limits.

Case 2

A housewife aged 50, known to have had mitral stenosis and auricular fibrillation without symptoms for at least one year, was seized on the evening of July 1, 1952, by severe pain in the front of the left leg. Two hours later her family doctor found diminished pulsation in the dorsalis pedis and posterior tibial arteries, and cutaneous anaesthesia of the toes on the affected side. He administered morphine. Two hours later the pain and anaesthesia had gone and pulsation was normal. The following morning, however, the pain and anaesthesia returned, the foot was cold, and dorsiflexion was impaired.

The following signs were present on the affected side when she was admitted to hospital that afternoon: the anterior tibial muscles were painful, slightly swollen, moderately indurated, tender to pressure and stretching, and paralysed; there was cutaneous anaesthesia of the first and second interdigital clefts, and the skin of the foot was cold and coloured a dusky pink; the dorsalis pedis and posterior tibial arteries did not pulsate, while those in the healthy leg were normal.

The next day there was a little return of movement, though the induration was greater. The temperature was 98.8° F. (37.1° C.) during the first week, and normal thereafter. The neutrophils numbered 13,800 per c.mm. in a total white-cell count of 17,000 during the first week; the E.S.R. was 28 mm./hour (Wintrobe). All affected muscles responded to faradism, but the current required was greater than normal. Peripheral pulsation became detectable during the third week; it always remained feeble and was sometimes impalpable. Fasciculation was seen in the affected muscles. During the ensuing weeks the tibialis anterior muscle remained hard, and limitation of plantar flexion suggested that this was due to fibrosis.

Two years later she was readmitted with a left hemiplegia, ascribed to cerebral embolism, from which she made a good functional recovery. It was noted that pulsation in both dorsalis pedis arteries was normal and equal.

Case 3

A chronic alcoholic barman aged 53 was admitted to hospital on March 3, 1957, with a history of melaena for two days. He was profoundly anaemic, the haemoglobin being 2.4 g./100 ml. (16% Haldane). The blood pressure was 120/60. Scattered crusted sores and skin pigmentation gave evidence of self-neglect. Three pints (1.7 litres) of blood was transfused. Two days later he had a severe recurrence of bleeding, the haemoglobin falling to 2.7 g./100 ml. (18% Haldane) and the blood pressure to 60/40. A further 5 pints (2.8 litres) of blood was transfused, and, as regards the intestinal bleeding, he made a fluctuating but ultimately good recovery on Hurst's dietary regimen, iron, and antacids. A barium-meal examination at the third week showed evidence of duodenal ulceration, but none of oesophageal varices.

On March 5, very shortly after the recurrence of bleeding and oligaemic shock, and before receiving his second transfusion, he complained of persistent cramp-like pain in the front of his left leg. Seven days later all muscles in the anterior tibial compartment were hard, tender, and paralysed; the overlying skin was a dusky red, and there was impaired cutaneous sensibility in the first interdigital cleft. A plaster back-slab was applied to correct the foot-drop. During the next four weeks the overlying skin became bright red, with extension of the discoloration to the dorsum of the foot. The entire anterior tibial muscle group underwent softening and was soon fluctuating. He had a number of pustules and boils in the scapular region and a large one on the right buttock, but there were none on the affected leg. Mr. A. N. McCrea made an incision 4 in. (10 cm.) long into the upper third of the fluctuating area. The compartment was evacuated, leaving a cavity bounded by tibia, fibula, and interosseous membrane. It contained pus, from which coagulase-positive *Staphylococcus aureus* was grown, and pink necrotic muscle having the consistency of blancmange. After a number of weeks the cavity was clean and lined by healthy granulations.

On June 4, he was transferred to St. Charles' Hospital with a view to skin grafting, but his general condition, at all times poor, deteriorated further. Mr. N. D. Ashe reported that an above-knee amputation was performed on August 7, and that this was followed by gangrenous patches on the right leg and later congestive heart failure, from which the patient died on September 29.

Case 4

A woman aged 77 was undergoing in-patient medical treatment for haematemesis due to gastric and duodenal ulceration. There was no shock or anaemia. She also had auricular fibrillation and left ventricular hypertrophy due to hypertension, uncomplicated by cardiac failure. A few days before admission she had been aphasic, but speech was almost normal when she was admitted on August 6, 1957.

Eleven weeks after admission she experienced pain in the left leg. On examination, 18 hours after the onset of pain, the left tibialis anterior muscle was tender, indurated, and paralysed. Pulsation was absent from the left dorsalis pedis artery. All other arteries of the lower limbs pulsated normally, the long extensor muscles were intact, and, so far as could be determined with her impaired co-operation, sensibility was likewise intact. The next day the skin overlying the tibialis anterior was reddened, the foot maintaining normal colour and temperature. Heparin was given initially and followed by a course of phenindione, but without noticeable benefit.

Biopsy of the tibialis anterior muscle was performed by Mr. N. Samuels nine days after the onset of crural symptoms. When the overlying fascia was incised dark blood oozed out. The infarcted muscle was a dark greyish blue and failed to contract on being cut. Three months later the induration, paralysis, and absence of arterial pulsation were unchanged.

Histological Findings

Examination of the biopsy specimen taken nine days after onset gave the following results. The two fragments consisted mainly of mature collagenous fibrous tissue in which were many small muscle fibres. These fibres showed a tendency to parallel arrangement but were widely separated by collagen. They varied greatly (from 6 to 38 μ) in diameter, and most of them had numerous sarcolemmal nuclei. Most of these fibres were deeply stained with Mallory's phosphotungstic acid haematoxylin and showed clearly the individual myofibrils, but transverse striae were visible only in a few. The ambient fibrous tissue was sparsely infiltrated by lymphocytes, and traces of free iron were found in it; recent extravasation of blood had occurred in some areas. The appearances suggested a slowly progressive ischaemic atrophy with replacement fibrosis and some regeneration of the muscle fibres.

At the edge of both fragments were a few small areas (the largest only 1.8 mm. in diameter) of architecturally intact muscle showing signs of recent necrosis. The fibres here were normal in diameter (40 to 52 μ) and many of them showed normal transverse striation, although the normal staining reaction with Mallory's phosphotungstic acid haematoxylin had been completely lost or greatly impaired. Some but not all of the sarcolemmal nuclei had disappeared. Extravasated red cells occurred in some of the endomysial spaces, but there was no leucocytic infiltration. The appearance of these small areas suggested acute ischaemic necrosis of very recent origin. The few arterioles and small arteries in the sections appeared contracted but structurally normal.

Case 5

A man aged 79 was admitted to hospital on November 7, 1957, having had a brief attack of impaired or lost consciousness earlier the same day. On admission he had fully recovered from the attack and was found to have gross left ventricular hypertrophy, a regular pulse of 38 a minute, a blood pressure of 130/75, and signs of right and left ventricular failure. Electrocardiography demonstrated complete A-V block. It seemed that the episode that occasioned his admission was either a Stokes–Adams or a "cerebrovascular" attack. He was digitalized and eventually made a satisfactory recovery from the failure.

On November 11 he developed acute bronchitis, for which he was given tetracycline. Two days later he complained of pain in the left leg. The front of the leg and the dorsum of the foot were cold and cyanotic. All arterial pulses on that side, other than the femoral, were absent. On the fourth day after the onset of pain in the leg the left tibialis anterior muscle was found to be hard, acutely tender to pressure and stretching, and paralysed; the other muscles were intact. Cutaneous sensibility was impaired in the first interdigital cleft. The skin over the tibialis anterior muscle was slightly reddened and that over the dorsum of the foot slightly cyanotic. He was given several injections of tolazoline and nylidrine hydrochloride ("perdilatal") into the femoral artery without benefit.

Mr. E. D. Morris performed a biopsy 10 days after the onset and described the tibialis anterior muscle as dark blue in colour. On incising it there was dark venous oozing. The muscle failed to contract on being pinched or cut. During the ensuing weeks the cutaneous erythema deepened and the induration and paralysis persisted. In January, 1958, lobar pneumonia developed, from which he died. Post-mortem examination by Dr. S. A. Kahn showed: thrombotic occlusion of the femoral artery distal to the origin of the profunda femoris; pneumonic consolidation of the left lower lobe; fibrosis of ventricular septum; left ventricular hypertrophy; and widespread atherosclerosis.

Histological examination of the biopsy specimen taken 10 days after the onset gave the following results. The material consisted of a fragment of necrotic muscle. The muscle fibres were abnormally hyaline and some of them were swollen. They stained deeply with Mallory's phosphotungstic acid haematoxylin, but most of them had lost their transverse striation. Nearly all of the sarcolemmal nuclei had disappeared. The endomysial spaces were infiltrated by polymorphonuclear leucocytes and contained a little granular basophilic debris and a few extravasated red cells. The section included a few very small arterioles, which were histologically normal.

Discussion

It was pointed out earlier that the anterior tibial syndrome can be caused by three different and unconnected agencies: (1) unaccustomed exertion involving the anterior tibial muscles in healthy subjects; (2) local exogenous mechanical factors causing a rise in pressure within the anterior tibial compartment; and (3) occlusion of the anterior tibial artery or a parent trunk by embolism or thrombosis.

In order to understand the peculiar vulnerability of the contents of the anterior tibial compartment we must consider its anatomy. The tibialis anterior, extensor hallucis longus, and extensor digitorum longus are contained within a relatively rigid compartment bounded by the tibia, fibula, interosseous membrane, and overlying fascia. The anterior tibial artery, veins, and nerve also lie within this compartment. The arterial supply of these muscles has been studied by the injection of radio-opaque suspensions (Blomfield, 1945, 1948; Hughes, 1948).

The tibialis anterior is supplied solely by the anterior tibial artery through a series of about 12 segmental branches except for the proximal third, which is also supplied by the anterior tibial recurrent artery. There is no effective anastomosis between these vessels. The extensor digitorum longus is supplied by the anterior tibial, and by three perforating branches of the posterior tibial and by the perforating peroneal arteries. These arteries anastomose within the muscle. The extensor hallucis longus is supplied by the anterior tibial and perforating peroneal arteries. According to Campbell and Pennefather (1919) intramuscular anastomoses are so fine that the main muscular branches can be regarded as end-arteries. Ligation of the anterior tibial artery at various levels below its point of entry into the compartment results in cutting off the supply to the muscles distal to the ligature. A localized occlusion of the anterior tibial artery is unlikely on anatomical grounds to cause necrosis of all three muscles, the long extensors being less vulnerable than the tibialis anterior. This is confirmed by clinical experience.

There is little doubt that, when the syndrome follows unaccustomed exertion post-exertional swelling of the muscles compresses the anterior tibial artery and its branches, obliterating their lumina. The muscular pain and stiffness that so commonly follow unaccustomed activity are probably due to oedema and microscopic haemorrhages within the muscle. A substantial increase in muscle volume can occur in these circumstances. Barcroft and Kato (1915) found that 15 minutes' intermittent faradic stimulation of a dog's gastrocnemius and digastric muscles, in a manner simulating normal activity, resulted eight hours later in a 19% increase in weight of the muscle due to oedema. Weight-lifting can cause in half an hour a temporary increase of as much as 1½ in. (3.8 cm.) in the circumference of the upper arm (MacQueen, 1954). Small interfibrillary and interfascicular haemorrhages may also occur (Lorenz, 1898; Meyenburg, 1929) and contribute to enlargement of the muscle.

A pressure of about 50–60 mm. Hg, much lower than that required to collapse the main artery, will, when exerted direct upon a muscle itself, collapse its capillaries and completely arrest the flow (Lewis, 1936). Where muscles are free to expand no harm is done. Expansion of the anterior tibial muscles, however, is limited by the relatively rigid walls of the compartment within which they lie. Comparatively slight swelling may therefore raise the pressure within the compartment enough to obliterate the blood supply. The perforating arteries which supply the long extensors run a shorter course within the compartment and are less subject to compression. Hence these muscles are less vulnerable.

When the syndrome is due to a local expanding lesion—for example, trauma or infusion of fluid—the effects of a rise in intracompartmental pressure are similar.

In cases of the third category, five of which are here reported, the effects of an arterial block by embolism or thrombosis and the extent of the infarction are dependent on the site of the block, on the degree of impairment of the collateral circulation by atherosclerosis, and on the amount of swelling in the muscle that follows its infarction. Post-infarctional swelling tends to obliterate collateral vessels and thereby increase the ultimate mass of necrotic muscle.

In Case 1 pulsation was present in the posterior tibial artery and absent from the dorsalis pedis artery, indicating a block in the anterior tibial artery. All muscles within the compartment were paralysed. Biopsy on the 11th day showed ischaemic necrosis. The piece taken 14 months later showed evidence of regeneration. The electrical reactions on the 35th day indicated neuropathic paralysis of those muscles which had not undergone necrosis. The return by the 60th day of contractility and faradic response to the greater part of the muscle group is attributable to recovery from the neuropathy and to regeneration in some of the necrotic muscle fibres. Regeneration has been reported in this syndrome by Pearson *et al.* (1948) and by Hughes (1948), and has been observed experimentally by Le Gros Clark (1946).

At the onset, transient pain was complained of in the opposite leg. This, too, may have been ischaemic and due to contralateral arterial spasm. Atlas (1942) has noted that in cases of embolic occlusion of a small artery of a lower limb the ensuing arterial spasm may be so widespread as to involve the opposite limb. Barnes and Trueta (1942) applied a tourniquet to a rabbit's thigh for several hours. In addition to widespread ipsilateral arterial spasm, they noted occasional spasm in the contralateral limb beginning at the same level as the tourniquet. Arterial spasm following embolism and its subsequent relaxation might explain the return of pulsation to the dorsalis pedis artery. The decubitus, with affected limb flexed at hip and knee, was also noted by Pearson *et al.* (1948), and its cause was discussed in the report on Case 1.

In Case 2 pulsation was absent from the posterior tibial and dorsalis pedis arteries on the affected side, indicating a block, clinically embolic, of the popliteal artery or its bifurcation; yet evidence of ischaemia was confined to the specially vulnerable muscles of the anterior crural group.

Case 3, ascribed to thrombosis, was remarkable for the liquefaction undergone by the contents of the compartment. As the skin overlying the compartment was not infected, the infection within was probably derived from one of the patient's many boils. No other foci were found. It is puzzling to see how blood-borne organisms could have reached an avascular region. Possibly they were in transit at the moment of infarction. Although arterial thrombosis presumably occurred on a basis of atherosclerosis, infarction was precipitated by profound anaemia and oligaemic shock. Bedford (1956) has reported cases of cerebral infarction following shock due to severe gastro-intestinal haemorrhage, and Master *et al.* (1950) have reported cases of myocardial infarction of similar origin.

In Cases 4 and 5 the patients were old, and cerebral and cardiac signs indicated the presence of widespread and severe atherosclerosis. Here arterial thrombosis was the immediate cause of the syndrome. The slowly progressive ischaemic atrophy and fibrosis seen histologically gave rise to no clinical signs.

Treatment

It seems logical to treat post-exertional cases by decompressing the compartment with a long incision dividing the deep fascia over the muscles. Promptitude is essential, as muscle deprived of its blood supply will undergo necrosis unless the ischaemia is relieved within a few hours of the onset of symptoms. Decompression after necrosis has occurred may aid regeneration. Despite the failure of limited medical measures in Cases 4 and 5, we suggest that the simultaneous administration of papaverine, nylidrine hydrochloride, and anti-coagulants offers hope of resolution in cases due to arterial thrombosis or embolism.

Summary

The clinical features of the "anterior tibial syndrome" are described. The main features are ischaemic necrosis of the tibialis anterior muscle and, in greater or less degree, the extensor hallucis longus and extensor digitorum longus muscles; these three muscles occupy the rigid-walled anterior tibial compartment. The immediate cause of the syndrome is occlusion of the anterior tibial artery or its parent trunk. This may be due to (1) swelling of the muscles following unaccustomed exertion, and consequent rise in intracompartmental pressure above the arterial blood pressure; (2) local expanding lesions within the compartment, with similar effect; and (3) embolism or thrombosis of the anterior tibial artery or its parent trunk.

Five cases are reported, of which two were due to embolism, one to thrombosis following haemorrhagic shock, and two to thrombosis associated with senile atherosclerosis.

Our thanks are due to the surgeons who obtained biopsy specimens of muscle.

References

Atlas, L. N. (1942). *Surg. Gynec. Obstet.*, **74**, 236.
Barcroft, J., and Kato, T. (1915). *Proc. roy. Soc. B*, **88**, 541.
Barnes, J. M., and Trueta, J. (1942). *Brit. J. Surg.*, **30**, 74.
Bedford, P. D. (1956). *Lancet*, **2**, 750.
Blomfield, L. B. (1945). *Proc. roy. Soc. Med.*, **38**, 617.
—— (1948). Quoted by Hughes (1948).
Campbell, J., and Pennefather, C. M. (1919). *Lancet*, **1**, 294.
Carter, A. B., Richards, R. L., and Zachary, R. B. (1949). Ibid., **2**, 928.
Clark, W. E. Le Gros. (1946). *J. Anat. (Lond.)*, **80**, 24.
Freedman, B. J. (1954). *Proc. roy. Soc. Med.*, **47**, 183.
Griffiths, D. Ll. (1940). *Brit. J. Surg.*, **28**, 239.
Horn, C. E. (1945). *J. Bone Jt Surg.*, **27**, 615.
Hughes, J. R. (1948). Ibid., **30B**, 581.

Lewis, T. (1936). *Vascular Disorders of the Limbs*, p. 37. Macmillan, London.
Lorenz, H. (1898). Die Muskelerkrangungen. In *Specielle Pathologie und Therapie*, ed. H. Nothnagel, XI band, III teil, 1 Abt. Hölder, Vienna.
MacQueen, I. J. (1954). *Brit. med. J.*, **2**, 1193.
Master, A. M., Dack, S., Horn, H., Freedman, B. I., and Field, L. E. (1950). *Circulation*, **1**, 1302.
Meyenburg, H. von (1929). In *Handbuch der speziellen pathologischen Anatomie und Histologie*, edited by F. Henke and O. Lubarsch, vol. 9, part I, p. 358. Springer, Berlin.
Pearson, C., Adams, R. D., and Denny-Brown, D. (1948). *New Engl. J. Med.*, **239**, 213.
Phalen, G. S. (1948). *Ann. Surg.*, **127**, 112.
Sirbu, A. B., Murphy, M. J., and White, A. S. (1944). *Calif. west. Med.*, **60**, 53.
Tillotson, J. F., and Coventry, M. B. (1950). *Proc. Mayo Clin.*, **25**, 223.
Vogt, P. R. (1943). Unpublished paper read before the Oregon State Medical Society on September 4, 1943. Quoted by Horn (1945).
Watson, D. C. (1955). *Brit. med. J.*, **1**, 1412.

HYPERCALCAEMIA AND RENAL FAILURE IN MULTIPLE SECONDARY CARCINOMA OF BONE

REPORT OF A CASE

BY

P. H. SANDERSON, M.B., M.R.C.P.

Medical Unit, St. Mary's Hospital, London

The association of hypercalcaemia and renal failure is familiar from such examples as hyperparathyroidism (Albright and Reifenstein, 1948; Cohen, FitzGerald, Fourman, Griffiths, and de Wardener, 1957), calciferol overdosage (Danowski, Winkler, and Peters, 1945), and sarcoidosis (Dent, Flynn, and Nabarro, 1953; McSwiney and Mills, 1956). It has also been described in secondary carcinoma of bone (Albright and Reifenstein, 1948; Swyer, Berger, Gordon, and Laszlo, 1950; Snelling, 1952; Couch and Lewis, 1953). The mechanism of the hypercalcaemia in the latter group of cases seems clear enough; it is generally agreed to be due to release of calcium into the blood stream through the destruction of bone by the secondary deposits of carcinoma. Agents which accelerate this process raise the serum calcium; agents which retard the process cause the serum calcium to return towards normal (Pearson, 1957). The mechanism of the renal failure is less certain. It might, for example, be due to the blocking of renal tubules by casts of calcium salts; on the other hand, rapid fluctuations of serum calcium level are sometimes followed so closely by corresponding changes in blood urea that this explanation seems improbable.

Detailed renal function studies in this condition have not often been made; those recorded here do not indicate the exact mechanism of the functional disorder, but because of the sparseness of such information they are presented in the hope that they will stimulate further observations.

Case Report

The patient was a married woman aged 49 whose periods had ceased three years previously. Four months before admission she noticed a swelling in the left breast. On examination a hard mass attached to the skin was found. This was removed at a radical mastectomy. Histology showed trabecular and solid alveolar polygonal-cell carcinoma, with extension to the axillary glands. She was given post-operative *x*-ray therapy to the chest wall and axilla.

Two months after the operation she began to notice pain in the lower back. *X*-ray films showed probable secondary deposits in the right ischium. Further *x*-ray therapy was given, to the pelvis and lumbar spine, and testosterone, 100 mg. twice weekly, was prescribed. Two weeks later the pain was much worse and the patient appeared mentally confused. Testosterone therapy was stopped, a total of 400 mg. having been given, and the patient was admitted to hospital on March 12.

On admission she appeared slightly confused and fatuous; cerebral secondary deposits were suspected, but there were no localizing neurological signs. An E.E.G. (Dr. Neil Gordon) was reported on as follows: "This record is grossly abnormal. The abnormalities were generalized and consisted of irregular moderate-voltage slow waves in both the theta and delta ranges. There was no regular alpha rhythm, and eye opening did not cause any significant change in the trace. In fact, the background of the record between the slow waves was remarkably flat. There was a slight increase in synchrony on overbreathing. Conclusions: The findings would be compatible with a gross generalized disturbance of cerebral function. The abnormalities were non-specific, but were so marked that if they were due to raised intracranial pressure one would have expected unequivocal clinical evidence of this. This raises the possibility that they are due to a metabolic disorder." Investigation of blood chemistry the next day showed alkalosis, potassium depletion, and uraemia (see Table).

Blood Chemistry

	March					
	13 V	14 V	15 A	17 A	19 V	20 V
Plasma sodium (mEq/l.) ..	139·5	—	140	138	—	—
Plasma potassium (mEq/l.) ..	3·4	—	2·9	3·1	4·55	4·8
Plasma chloride (mEq/l.) ..	91·0	—	94·0	100·0	—	—
Plasma total CO_2 (mEq/l.) ..	38·0	—	34·0	27·3	—	—
Blood pH ..	—	—	7·47	7·465	—.	—
Blood urea (mg./100 ml.) ..	150	—	149	122	106	—
Serum calcium (mg./100 ml.)	—	16·6	16·6	14·2	13·0	12·5
Serum inorganic phosphorus (mg./100 ml.)	—	—	4·5	4·7	—	—

A = Arterial. V = Venous.

The elevated plasma urea, coupled with probable secondary deposits in the skeleton, raised the possibility of hypercalcaemia; the serum calcium was found to be 16.6 mg./100 ml. Subsequent blood chemistry results are shown in the Table and the Chart. The alkalosis and potassium depletion were corrected by the administration of 4 g. of potassium chloride daily: by March 20, when the serum potassium was 4.8 mEq/l., a total of 96 mEq of potassium had been retained, suggesting that originally the potassium depletion was of slight degree only. As may be seen, the serum calcium and blood urea levels fell steadily; the former reached a normal figure by March 27, but the blood urea continued to be moderately raised.

A further E.E.G. on March 18, when the potassium depletion had been nearly, and the alkalosis fully, corrected, but when the serum calcium was still elevated, showed great improvement but was still not quite normal, with poorly formed alpha rhythm and little change on eye opening. The patient's mental state at this stage appeared quite normal. E.E.G. examinations on March 26 and April 2 showed further improvement, the last record being reported as completely normal.

Renal function was studied during the episode by the following techniques. (1) Urine specimens were collected (*a*) after 12 hours' water restriction, and (*b*) after two units of pitressin tannate intramuscularly, and the osmolality was measured by a modified Hill-Baldes vapour-pressure apparatus; the maximum value was recorded. (2) Inulin clearances and PAH Tm rates were measured by the usual techniques (Smith, 1956). (3) The maximum rate of tubular reabsorption of solute-free water (Tm $\frac{C}{H_2O}$) during a mannitol diuresis was measured (Smith, 1956). PAH Tm was measured in preference to the clearance in view of the doubtful significance of clearance figures when gross renal failure is present. The results are shown in the Chart below.

Urine concentrating power, as measured by the maximum osmolality of the urine, was extremely low at the onset; this urine had a specific gravity of 1009. There was a marked improvement to nearly normal figures during the period of observation, the specific gravity rising to 1019. Inulin clearance increased from a low level to a still subnormal figure; PAH Tm (in mg. per minute) was at first very low indeed, and rose to a figure a little over half the normal (77 mg./min.). The quotient $C_{IN} \div TmPAH$ was successively 8.4, 1.4, and 1.4, the last two being normal ratios, which suggests that during the period of recovery glomerular and tubular functions were affected equally, but that at the time of the first study, when the serum calcium was still 11.5 mg./100 ml., tubular function was affected much more severely than glomerular. The figures from Tm $\frac{C}{H_2O}$ indicate gross depression of this function with incomplete recovery, the normal value being 5–6 ml./min.

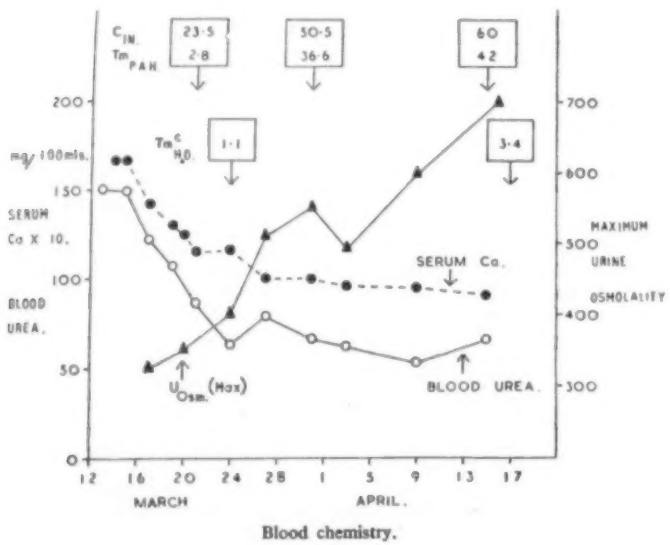
With the object of suppressing possible adrenal oestrogen, 50 mg. of prednisone daily was administered from March 27 onwards. This did not seem to alter the trend towards recovery of renal function. The last observations on the latter during this admission were made on May 16, when the maximum urine osmolality was 690 m.Osm./kg. (S.G. 1020). Serum calcium on the previous day was 9.7 mg./100 ml. and the blood urea was 47 mg./100 ml. The patient received further *x*-ray therapy to the lumbar spine between May 23 and June 4, and was discharged on June 10 fairly comfortable, though still complaining of some pain in the lower back. Further *x*-ray films had shown multiple small osteolytic metastases in the right ischium, above both acetabula, in the intertrochanteric regions of both femora, and in the neck of the right humerus. Over the period April 10 to 15, the average daily calcium intake was 230 mg., and the urinary calcium output varied between 38 and 58 mg. a day, suggesting that at this stage the metastases were relatively inactive.

She was readmitted on June 23 in severe pain with a serum calcium of 12.8 mg./100 ml. and a blood urea of 69 mg./100 ml. The maximum osmolality was now 390 m.Osm./kg. (S.G. 1012). Her condition deteriorated rapidly and she died two weeks later.

Permission for a full post-mortem examination was unfortunately not obtained. Removal of one kidney was, however, allowed; it was normal macroscopically, and the microscopical report (Dr. R. H. Heptinstall) was as follows: "On the whole this is a surprisingly healthy kidney, with very little glomerular loss or in fact glomerular changes. The proximal tubules apart from showing post-mortem change appear healthy. There is some equivocal evidence of regeneration in the distal nephrons, although this is difficult to assess. Some of these show calcification and there is a moderate amount of calcification in the interstitium. Some casts are also present in these tubules. The amount of calcification is nowhere near as great as I have seen in these cases, but it is undoubtedly present. If the calcium deposition was originally responsible for the impairment of renal function then it must have regressed to a considerable extent, unless derangement of calcium metabolism acts on the kidney in a way independent of gross calcium deposition."

Discussion

Deterioration of patients with cancer of the breast and metastatic deposits in bone when testosterone is administered is a well-recognized though fortunately rare phenomenon (Nathanson and Kelley, 1952), and has been ascribed to the conversion *in vivo* of testosterone to an oestrogen (Wotiz, Davis, Lemon, and Gut, 1956). In the present case the hormonal stimulation of the secondary deposits led to a rise in serum calcium and a profound disturbance of all the renal functions studied. Some of these, such as the power to form concentrated urine, made a good recovery towards normal; others, including the power to excrete urea, recovered more slowly and apparently only partially. Observations in patients with hyperparathyroidism (Cohen *et al.*, 1957) indicate that tubular water reabsorption is affected to a marked extent in this condition, and recovers on removal of the parathyroid adenoma, though whether this is an effect of parathyroid hormone or of calcium is not clear. Studies on experimental renal calcification in rats (Sanderson, 1959) also suggest that tubular water reabsorption is easily disturbed by a high intake of calcium, and that it recovers rapidly when the calcium intake falls, even if the amount of calcium deposited in the kidney remains unchanged. In these experiments, also, the power to excrete urea recovered much less readily than the power to produce concentrated urine.



Blood chemistry.

The actual mechanism of these changes remains obscure. Dr. Heptinstall's comment on the kidney histology at post-mortem examination suggests that there may be some mode of action of calcium other than that of causing tubular blockage, an idea in line with my experimental studies already quoted and with the marked polyuria in hyperparathyroidism, with hypotonic

urine, observed by Cohen *et al.* (1957). But the simple mechanical effect of tubular blockage is obviously not ruled out, and the solution of the problem must await further observation on similar cases, if possible with renal biopsy at the height of the hypercalcaemia.

The reason for the mental confusion and the E.E.G. changes is not clear. Mental changes, in the shape of confusion and hallucinations, have been occasionally described in hypercalcaemic states, but they are decidedly uncommon. Fitz and Hallman (1952) have given a particularly clear description of two cases of hyperparathyroidism in which mental abnormalities were present. Mental changes are common, however, in the combination of alkalosis and hypercalcaemia which may complicate the medical treatment of peptic ulcer (Wenger, Kirsner, and Palmer, 1957). Alkalosis alone causes no mental change (van Goidsenhoven, Gray, Price, and Sanderson, 1954). The present patient, besides hypercalcaemia, had a mild alkalosis, and it is possible that it is the combination of these two factors which is capable of causing mental abnormalities.

Summary

A case of carcinoma of the breast with secondary deposits in bone, in which the condition was made worse by testosterone therapy, is described. Hypercalcaemia, mental confusion, and uraemia developed; the abnormalities of renal function were studied in some detail.

I am grateful to Sir Arthur Porritt for permission to publish this case, and to Mr. J. Fawcett for help with the Tm $\mathfrak{G}_2O$ determinations.

REFERENCES

Albright, F., and Reifenstein, E. C. (1948). *The Parathyroid Glands and Metabolic Bone Disease*. Williams and Wilkins, Baltimore.

Cohen, S. I., FitzGerald, M. G., Fourman, P., Griffiths, W. J., and de Wardener, H. E. (1957). *Quart. J. Med.*, **26**, 423.

Couch, R. S. C., and Lewis, A. A. G. (1953). *Arch. Middx Hosp.*, **3**, 84.

Danowski, T. S., Winkler, A. W., and Peters, J. P. (1945). *Ann. intern. Med.*, **23**, 22.

Dent, C. E., Flynn, F. V., and Nabarro, J. D. N. (1953). *Brit. med. J.*, **2**, 808.

Fitz, T. E., and Hallman, B. L. (1952). *A.M.A. Arch. intern. Med.*, **89**, 547.

McSwiney, R. R., and Mills, I. H. (1956). *Lancet*, **2**, 862.

Nathanson, I. T., and Kelley, R. M. (1952). *New Engl. J. Med.*, **246**, 135.

Pearson, O. H. (1957). *Cancer*, **10**, 799.

Sanderson, P. H. (1959). *Clin. Sci.*, **18**, 67.

Smith, H. W. (1956). *Principles of Renal Physiology*. Oxford Univ. Press, New York.

Snelling, M. D. (1952). *Arch. Middx Hosp.*, **2**, 32.

Swyer, A. J., Berger, J. S., Gordon, H. M., and Laszlo, D. (1950). *Amer. J. Med.*, **8**, 724.

van Goidsenhoven, G. M.-T., Gray, O. V., Price, A. V., and Sanderson, P. H. (1954). *Clin. Sci.*, **13**, 383.

Wenger, J., Kirsner, J. B., and Palmer, W. L. (1957). *Gastroenterology*. **33**, 745.

Wotiz, H. H., Davis, J. W., Lemon, H. M., and Gut, M. (1956). *J. biol. Chem.*, **222**, 487.

The Research Defence Society, which was founded in 1908 to "make known the facts about experimental research involving the use of animals . . . and to defend research workers in the medical, veterinary and biological sciences, against attacks by anti-vivisectionists . . ." has published "Surgery of the Heart and Circulation" in its Conquest Pamphlet Series (No. 7, price 6d.).

BREAST ABSCESS AS A THREAT TO SURGICAL UNITS IN A GENERAL HOSPITAL

BY

J. G. P. HUTCHISON, M.D.

Lecturer, Department of Bacteriology, University of Glasgow

Breast abscess is most often a post-partum condition. If confinement takes place in a maternity hospital the organism responsible, *Staphylococcus aureus*, will most often be one of the antibiotic-resistant types prevalent there. Disease does not, however, usually supervene until some weeks after the patient's discharge from the unit. Thus the harvest of disease is reaped in hospitals far removed from that in which it was sown and by different medical hands. With the prime purpose of finding out which maternity hospitals were producing what kinds of staphylococci and reporting the findings back to their origin, a survey was made of the cases of breast abscess admitted for surgical treatment to the Western Infirmary, Glasgow, during 1958.

Material Studied

From pus obtained at operation on 75 patients, 75 strains of *Staph. aureus* were isolated, duplicate specimens being excluded. The antibiotic sensitivity to penicillin, streptomycin, chloramphenicol, the tetracyclines, and erythromycin was tested with Evans's "sentests." Phage-typing (Williams and Rippon, 1952) was carried out on 70 of the 75 strains. From 46 of the 75 cases I learned as much as I could by direct questions to the patient—for example, whether puerperal or not, the hospital of confinement, and drug therapy before admission ("known history group"). In non-puerperal cases, only those abscesses arising *de novo* were included.

Findings: Antibiotic Sensitivity Patterns

Crude data on antibiotic sensitivity of all 75 strains of staphylococci are given in Table I. Only 11 (15%) were sensitive to all antibiotics. Forty-six of the strains came from patients with a known history, and 8 (17%) of them were sensitive to all antibiotics. The similarities of sensitivity pattern between staphylococci from patients with known and those with unknown history permit the assumption that the 29 cases of unknown history belong to the same statistical population as the other 46.

The "known history" group has been divided into puerperal and non-puerperal cases. All the puerperal patients had been confined in maternity units. Of the eight non-puerperal strains, 6 (75%) were sensitive to all antibiotics and 2 (25%) were resistant to penicillin alone. Of the 38 puerperal strains, however, only 2 (5%) were completely sensitive and 22 (58%) were resistant to penicillin alone. The polyantibiotic-resistant nature of the latter strains is striking. The difference between the number of strains sensitive to penicillin in the two above groups of women is highly significant ($t=4.46$; $P<0.001$) and supports the idea of a fundamental difference in origin of their staphylococci.

Phage Types

The phage type in 70 of the 75 strains, together with the sensitivity reaction, is given in Table II. A great

TABLE I.—*Antibiotic Sensitivity of Strains of Staph. aureus from Breast Abscesses During* 1958

	Sensitive	Resistant						Total Strains
	PSCTE	P	PS	PST	PT	PSCT	PSTE	PE	
Crude intake, 1958	11 (15%)	39 (52%)	5 (7%)	8 (11%)	8 (11%)	1 (1%)	2 (3%)	1 (1%)	75
" " known history ..	8 (17%)	24 (52%)	3 (7%)	2 (4%)	5 (11%)	1 (2%)	2 (4%)	1 (2%)	46
Puerperal	2 (5%)	22 (58%)	3 (8%)	2 (5%)	5 (13%)	1 (3%)	2 (5%)	1 (3%)	38
Non-puerperal	6 (75%)	2 (25%)	0	0	0	0	0	0	8

Note that in the "Resistant" columns omission of a drug indicates sensitivity to it. P=Penicillin. S=Streptomycin. C=Chloramphenicol. T=Tetracycline. E=Erythromycin.

diversity of lytic pattern is seen, no doubt due to the number of different maternity units (at least 10) from which the staphylococcal strains were derived. However, the arresting feature is the occurrence of 27 (39%) type 80 and 52/52A/80 strains amongst the 44 of phage-group I. It will be seen that the majority of the polyantibiotic-resistant staphylococci belong to these two phage types. Of the 27 strains, 6 (22%) were sensitive to chloramphenicol and erythromycin only; 8 (30%) were sensitive to streptomycin, chloramphenicol,

TABLE II.—*Phage Type and Sensitivity of Staphylococci Obtained from Breast Abscesses in* 1958

	No. of Strains	Sensitive	Resistant					
		PSCTE	P	PS	PST	PT	PSTE	PE
Total group I	44							
80 ..	11	—	3	2	1	3	2	—
52 52A/80	16	—	4	2	5	5	—	—
Others	17	4	12	1	—	—	—	—
Total group II	3	2	1	—	—	—	—	—
" III ..	7	1	6	—	—	—	—	—
Unclassified ..	4	1	3	—	—	—	—	—
Mixed groups	4	1	1	—	2	—	—	—
N.T. strains	8	2	5	—	—	—	—	1
Total ..	70	11	35	5	8	8	2	1

and erythromycin; 2 (7%) were sensitive only to chloramphenicol and none was resistant to this drug. These strains came from six (or more) widely separated maternity units and did not represent the result of a single epidemic in one. It may be noted that the liability to become resistant to a number of antibiotics, which is a well-known property of phage-group III staphylococci, was not demonstrated in the present series of seven strains.

The close association of types 80 and 52/52A/80 in the matter of antibiotic resistance does not seem to be a coincidence, for occasional variation appears to occur from one phage type to the other. For instance, two specimens were obtained from a single abscess in one patient at a seven-day interval; the first strain was type 52/52A/80, the second was type 80 alone; both strains had identical antibiograms. Cross-infection is unlikely, since, so far as is known, there was no other type-80 case in the ward at the time. Furthermore, in observations (unpublished) on nasal carriers of type 80, a change to type 52/52A/80 has sometimes been seen. Although this kind of evidence is open to more than one interpretation, it is felt that both these phage types should be regarded as having similar potential properties and that even if type 52/52A/80 is not itself as virulent as type 80, as the data of Williams (1959) suggest, the possibility of its changing to the more virulent type should be taken into account in epidemiological work.

Drug Therapy

In 25 cases the patient's history was thought to be reliable enough to determine therapy before hospital admission. Of these 25, 16 (64%) had had penicillin for periods ranging from two days to two weeks. From one non-puerperal case the organism was sensitive to penicillin, but the patient did not think that the drug had any effect, nor did it obviate the need for surgery. This patient had a history of infection for three days before penicillin therapy. Many of the patients whose staphylococci were subsequently found to be resistant stated that temporary relief was occasioned by penicillin.

Five patients were treated with one of the tetracyclines and in four the organisms were sensitive. In two of the latter cases tetracycline was given for one or two days only. Again, despite sensitivity of the staphylococcus to this drug, in two cases it failed to cure although an adequate dosage was given.

Four patients had no antibiotics, but from 10 (40%) a history of stilboestrol medication was obtained. The rationale of the latter in two cases appeared to be cracked nipples (which may predispose to infection). The other eight women did not wish to continue breast-feeding.

Discussion

A number of important points arise from these simple facts. Firstly, the maternity hospital medical staffs are largely unaware of the size of the problem, for patients do not return to them for surgical treatment, nor is there any mechanism for notification of disease of this sort stemming from the maternity unit. There would appear, therefore, to be a strong case for statutory notification of post-partum infections occurring within, say, six to eight weeks of confinement.

Secondly, the problem may not seem grave to any one surgeon in a general hospital because he sees relatively few of the total hospital intake. If he discovers the maternity unit of origin the surgeon may not be impressed owing to the wide scatter of patients from such units. In the present series, confinements took place in 10 entirely separate units, and this figure might well have been greater. Therefore the collected cases represent an unknown proportion of the total cases occurring from any one maternity hospital. There are here five large and many smaller hospitals to which patients with breast abscesses could be admitted, and so it is quite possible that in this area several hundred breast abscesses come to surgery each year.

A third point concerns the intake of breast abscess cases into general hospital wards. Their potential danger to other patients and to the hospital staff cannot be overemphasized (see Duthie, 1957). Thus a case of breast abscess may be found lying in the bed adjacent to a patient who is to undergo thoracotomy. The surgeon in whom a type-80 strain becomes entrenched may become the subject of recurrent boils; he is then an undoubted danger to his patients (McDonald and Timbury,

1957) or a loss to his profession, a latter-day leper to his family, and a misery to himself. Especially with the polyantibiotic-resistant type-80 strains, we have both virulence and resistance to therapy, which Rountree and Beard (1958) postulate as a reason for their pandemic spread. The question of isolation of these cases has been raised, but isolation, in this and many other hospitals, is almost impossible and a grave burden to the nursing staff if it is to be effective.

During the past decade or two the fever or isolation hospitals have fallen increasingly into disuse. It would seem sensible to transfer cases of ex-maternity hospital breast abscess to "fever" units rather than admit them to general wards. It is here the established practice to rush a case of meningococcal or pneumococcal meningitis off to isolation hospital—yet these conditions are infectious to a very limited degree, the causative bacteria respond to chemotherapy, and the patient requires urgent treatment which is quite unnecessarily delayed. Our thinking and regulations must move with the times if they are not to be the mere appendages of medieval folklore.

The treatment of breast abscess with antibiotics must also be considered. In the cases reviewed 16 out of 25 had received penicillin. It may be argued that these were "failed cases" selected out of a large group which never came to surgery, that they were fortuitously due to resistant staphylococci, and that failure of therapy was thus inevitable. The non-puerperal patients, however, constitute a small control group from whom the staphylococci were predominantly penicillin-sensitive; and one of these was known to have been given penicillin without effect. There is a common complaint among surgeons—for example, Mills (1953), Stammers (1953), Donald (1956), and De Jode (1957)—that penicillin therapy results in a surgically difficult and deplorable condition which mimics lactational cancer—the "penicillinoma."

Furthermore, it is apparent from the present observations and from maternity hospital studies (Duncan and Walker, 1942; Colbeck, 1949; Ludlam, 1953; Barber and Burston, 1955; Rountree *et al.*, 1956; Hutchison and Bowman, 1957; Monro and Markham, 1958) that the chance of a post-partum breast abscess being due to a penicillin-sensitive organism is very small, in contradistinction to the non-puerperal abscess. If, therefore, it is decided to give an antibiotic, then penicillin should *not* be amongst the drugs of choice. Indeed, it may be doubted whether the use of any antibiotic does any good at all, since it fails to cure once a mass has formed (Sawyer and Walker, 1954; Monro and Markham, 1958), and this seemed to happen within 24 to 48 hours of the initial symptoms in many of the present cases. Is it not also, apart from consideration of the patient, a waste of drugs and of public money to give antibiotics in inadequate dosage or for the inadequate period of one or two days? When patients with breast abscesses are discharged from hospital the general practitioner should be given the sensitivity of the organism isolated. This practice is by no means as universal as it should be, but it is very important in the case of recurrent disease in the patient or her child.

Finally, it may be noted that in the present cases, as in those of Mills (1953) and De Jode (1957), the temporary symptomatic relief of the patient under penicillin therapy cannot be taken as necessarily indicating sensitivity of the responsible organism.

Summary

Data are given on 75 cases of breast abscess admitted to a large general hospital during 1958. These data included sensitivity to antibiotics, phage type of staphylococci isolated, and the patient's history before admission.

The majority of strains came from women confined in hospital. Only 5% of these were fully sensitive to the antibiotics. Many of these strains were resistant to two or more antibiotics, and the phage types of the latter strains were predominantly types 80 and 52/52A/80. Conversely, in the non-puerperal group the majority of strains were fully sensitive and no strain was resistant to two or more antibiotics.

It is suggested that cases of puerperal breast abscess from maternity hospitals should be removed to an infectious disease hospital rather than be nursed in general surgical wards. A plea for notification of post-partum infections is made.

The apparent use of penicillin as the first line of defence in these cases is deprecated.

I am indebted to Mr. D. B. Colquhoun for technical assistance, also to numerous members of the hospital surgical and nursing staff for their co-operation and interest during the survey.

REFERENCES

Barber, M., and Burston, J. (1955). *Lancet*, **2**, 578.
Colbeck, J. C. (1949). *Can. med. Ass. J.*, **61**, 557.
De Jode, L. R. (1957). *Lancet*, **1**, 560.
Donald, I. (1955). *Practical Obstetric Problems*, p. 474. Lloyd-Luke, London.
Duncan, J. T., and Walker, J. (1942). *J. Hyg. (Camb.)*, **42**, 474.
Duthie, E. S. (1957). In *Hospital Coccal Infections*, p. 23. London.
Hutchison, J. G. P., and Bowman, W. D. (1957). *Acta Paediat. (Uppsala)*, **46**, 125.
Ludlam, G. B. (1953). *J. Hyg. (Camb.)*, **51**, 64.
McDonald, S., and Timbury, M. C. (1957). *Lancet*, **2**, 863.
Mills, C. P. (1953). *Brit. med. J.*, **1**, 1427.
Monro, J. A., and Markham, N. P. (1958). *Lancet*, **2**, 186.
Rountree, P. M., and Beard, M. A. (1958). *Med. J. Aust.*, **2**, 789.
—— Isbister, J. S., Dods, L., Cook, C. E., and Mays, B. T. (1956). Staphylococcal Infections in Maternity Hospitals. National Health and Medical Research Council, Special Report, No. 7. Canberra.
Sawyer, C. D., and Walker, P. H. (1954). *Surg. Gynec. Obstet.*, **99**, 368.
Stammers, F. A. R. (1953). *Brit. med. J.*, **1**, 272.
Williams, R. E. O. (1959). *Lancet*, **1**, 190.
—— and Rippon, J. E. (1952). *J. Hyg. (Camb.)*, **50**, 320.

QUEEN ELIZABETH, the Queen Mother, patron of the Queen's Institute of District Nursing, reviewed about 3,400 district nurses in the grounds of Buckingham Palace on July 1. The nurses had come from all parts of the United Kingdom and Eire, from Bermuda, Canada, Jamaica, Malta, South Africa, Tanganyika, and America to celebrate the centenary of their organization. The oldest nurse present was Miss AGNES DE FROISSARD, who is 92, and who attended a garden party and inspection by Queen Victoria at Windsor 63 years ago. Her Majesty presented a Gold Badge, the Institute's highest award, to Miss N. M. DIXON, deputy general superintendent of the Institute, "in recognition of her distinguished career as a Queen's Nurse for 32 years . . . ," and in her address referred to the district nurse as a familiar and well-loved figure, saying, "In a time when so much of our lives seems to be ruled by the telephone and the printed form you restore the personal touch."

TREATMENT OF TUBERCULOSIS OF THE SPINE

BY

M. C. WILKINSON, M.B., B.S., F.R.C.S.
Orthopaedic Surgeon, Black Notley Hospital, Braintree, Essex

The decline in the incidence of bone and joint tuberculosis in this country and in many others should not lead us into the error of thinking that this disease is no longer a problem of major importance, because there are large areas of the world where it is still one of the chief causes of death and crippling. Even in this country the figures are by no means negligible. In the four years 1955–8 the annual admissions to Black Notley Hospital of cases of tuberculosis of the spine of fairly recent origin were 40, 32, 26, and 20 respectively. During the same period the annual admissions of cases of old-standing spinal disease in need of further treatment were 9, 9, 13, and 13. The utmost that can be achieved by modern treatment is necessary for these patients. Up-to-date therapy should be combined with the old techniques which have been proved by experience and which are too valuable to be discarded. Constitutional treatment and skilled splintage are still essential to produce the best and quickest results.

In addition to constitutional treatment, posterior fusion has been a popular method of internal fixation of the spine, but any benefit that this produces must be an indirect one, and surgeons have never denied that the removal of sequestra and the drainage of abscesses is the method of choice in dealing with inflammatory diseases of bone. Unfortunately, radical surgical treatment of tuberculous osteomyelitis was risky until the introduction of antibiotics, as miliary tuberculosis or tuberculous meningitis might be precipitated by operation, with fatal results. An important investigation which emphasized the need for the direct treatment of the paravertebral abscess or granuloma was that of Swett, Bennett, and Street (1940). They published the results of the treatment of 350 patients suffering from spinal tuberculosis and came to the conclusion that the dominant feature in the healing of the disease lay in the "occurrence, behaviour, and disposal" of the abscess, and that it would be good surgical practice to undertake early aseptic evacuation of the abscess.

As the result of favourable experience of the direct operative treatment of tuberculous lesions in peripheral joints I had come to a similar conclusion, and in 1942 Sir Heneage Ogilvie operated with me on a child with gross and advancing spinal disease, it being thought worth while to take the risk of dissemination. The abscess was drained by the costotransversectomy route. The operation did not save the child's life, and it was not until the introduction of streptomycin in 1948 that this work was resumed.

Results Before Use of Antibiotics

Before considering the results of treatment of the spinal lesion by direct surgery, it will be of value to recall the degree of success obtainable before antibiotics became available. Table I shows the follow-up results in 131 out of a series of 340 patients treated at Black Notley during the years 1931–47. It will be seen that in 40 out of 51 patients treated for disease in the lumbar spine the result was good. In contrast, only 37 out of 75 patients treated for disease in the mid and lower thoracic and thoraco-lumbar regions got a satisfactory result. It should be noted that this table includes only patients who had a recent follow-up record, and does not include 209 whose records were incomplete or who had died. The inadequacy of constitutional treatment for a large number of patients with disease of the mid and lower thoracic spine, shown in Table I, is confirmed from the publications of such workers as Butler (1935), Dobson (1951), and Griffiths, Seddon, and Roaf (1956), all of whom reported that the maximum incidence of paraplegia followed disease in the mid and

TABLE I.—*Follow-up Results of* 131 *out of* 340 *Patients, Treated During* 1931–47 *for Tuberculosis of Spine Without Antibiotics or Operation*

Site of Lesion	Stable or Bony Ankylosis			Unsound Ankylosis		
	<15 Years	15+ Years	Total	<15 Years	15+ Years	Total
Lumbo-sacral ..	1	3	4	—	1	1
Lumbar	12	24	36	3	7	10
Thoraco-lumbar	3	14	17	5	5	10
Lower and mid-thoracic ..	7	13	20	12	16	28
Upper thoracic ..	1	—	1	1	—	1
Cervical	1	1	2	1	—	1
	25	55	80	22	29	51

lower thoracic vertebrae. This area is also associated with the development of gross deformity, especially in young children. Therefore it seemed clear, when antibiotics became available, that the main target of direct operation should be the mid and lower thoracic areas.

In 1948 I operated on two men who had tuberculosis of the thoracic spine, and in 1949 on two children with thoracic vertebral disease. My colleague, Mr. Ronald Reid, also operated in 1949 on a woman with lumbar vertebral disease. These patients were given only minimal streptomycin cover—namely, a small dose of the antibiotic twice a day for three weeks. Nevertheless, they suffered no ill effects and the results were most encouraging. Among the lessons learnt from these early operations were that progressive bone destruction could be stopped by operative intervention, and that to ensure a stable spine at the end of treatment the operation must be' done before gross vertebral destruction occurs, especially in children, in whom destruction of tuberculous bone may be rapid. A considerable improvement in the patient's general condition was also noted after operation, and there was a tendency for associated lesions, such as pulmonary disease, to heal.

Present Series

During the period 1948 to 1958 inclusive, 138 operations were performed on 128 patients. In most instances antibiotic cover was given for 14 to 18 weeks. Provided that no bone destruction is occurring, an interval of three to four months is allowed to elapse before operation in the case of adults; in children the interval is shorter. Operation then becomes easier and safer because inflammatory hyperaemia is less. Experience has shown that a paravertebral abscess in a child's spine may resolve as the result of antibiotic treatment, but the process is uncertain and may be incomplete, while the drainage of such an abscess leads to rapid and complete healing. The vertebrae of young children are small and the paravertebral abscess is the major factor to be dealt with. In adults, on the other

hand, drainage of the abscess, though necessary, is insufficient and curettage of the intravertebral granuloma is also required; sometimes the side of the vertebral body has to be removed to obtain access to the interior. Adult patients have been kept in their plaster beds for four months after operation, children for longer.

Tables II, III, and IV give particulars of the patients treated by direct operation on the spinal lesion. All patients operated on for secondary septic infection of the spine or for Pott's paraplegia have been excluded from this series. The operative mortality was nil (Table II). The most important operative complication, which has been encountered twice, was tension pneumothorax, due to puncturing the pleura, which may be softened and adherent. Great care is required, therefore, in getting out the rib heads; this may be difficult, as they may have developed an ankylosis to the vertebral bodies. A frequent sequel to the operation is a mild pleurisy or pleural effusion. When applying the dressing I make a practice of strapping the affected side a little. The patients have stood the operation well. For successful and safe operating two things are essential: first, a high degree of anaesthetic skill, because, if the patient gets anoxic, oozing occurs, impairing vision of the operative field; and, secondly, a high standard of bone radiography, because the definition of the abscess and of cavities and sequestra may be difficult even with good radiography. Quite marked cavitation and sequestration may be present without *x*-ray evidence, and it is also possible to operate for an apparent cavity and to find that it is not there.

TABLE II.—*Number of Patients Treated for Tuberculosis of Spine by Direct Operation on Lesion and Number of Operations Performed*

No of patients discharged 1948–58, inclusive	128
,, ,, direct operations performed on these patients	138
,, ,, patients with recent follow-up	125
Patients without recent follow-up	3*
Operative mortality rate	0

* Two died (one of non-specific pneumonia three years after discharge and one of tuberculous meningitis three years after discharge) and one emigrated.

TABLE III.—*State of Lesion on Follow-up of 128 Patients with 130 Spinal Lesions Treated by Direct Operation. Eight Patients Had Two Operations on Initial Lesions and Two Had Operations on Two Spinal Lesions*

Duration of Follow-up	Bony Ankylosis	Stable Fibrous Ankylosis	Unstable Fibrous Ankylosis
10 years	2		
9 ,,	1		1
8 ,,	4	3	
7 ,,	6	3	1
6 ,,	7	2	1
5 ,,	23	5	
4 ,,	12	6	
3 ,,	9	4	1
2 ,,	8	4	1
1 year	7	7	2
<1 ,,	3	6	1
Total	82	40	8

TABLE IV.—*Follow-up Results of 128 Patients with 130 Lesions Treated by Direct Operation, Grouped According to Situation of Lesion*

Area of Disease	Sound Healing with Stable Ankylosis, Bony or Fibrous	Unstable Ankylosis
Lumbo-sacral	31	3
Lumbar	6	2
Thoraco-lumbar	83	5
Lower and mid-thoracic		
Upper thoracic		
Total	120	10

The results shown in the tables were obtained in spite of the fact that many of the patients, especially in the first years, were selected for operation on account of severe disease for which orthodox methods of treatment had failed. The eight patients who are reported to have recovered with unstable fibrous ankylosis (Table III) include some who had extensive vertebral destruction but who improved to the extent that they were leading normal and useful lives. Concerning those classified as having bony or stable fibrous ankylosis, the distinction is sometimes invidious and difficult to determine. Under the heading "stable fibrous ankylosis" are included a type of result not often seen formerly—namely, re-formation of the vertebral bodies and considerable restitution of the intervertebral joint space.

These tables also show that the majority of patients treated by direct operation on the lesion had disease of the mid and lower thoracic and thoraco-lumbar portions of the spine—that is, the areas where poor results were formerly frequent. In spite of the unfavourable site of the lesions, most of these patients got an excellent result. They were selected for operation because it was felt that otherwise their prognosis was poor. They should be compared with another group of patients, shown in Table V, most of whom had disease in the lumbar region, for whom the prognosis was considered to be satisfactory without operation. There were 105 of these patients, treated over the same period of time as the operated patients. It is seen that the patients with disease in the lumbar region, with the exception of the 34 patients (Table IV) who were operated on, did well with conservative treatment and antibiotics only. The patients with disease in the thoracic portion of the spine (Table V), although they had been spared operation, as it was thought it was not necessary, fared less well than the more severe group who were operated on.

Table VI shows the number of patients who required readmission for further treatment. This was by no means a negligible proportion, and it follows that the treatment of spinal tuberculosis is still fraught with problems and difficulties. On the other hand, many of these patients had very severe disease, operated on in the early days as a last resort. Two of the patients in the series were readmitted with Pott's paraplegia—one

TABLE V.—*Results of Treatment of 105 Patients, Most of Whom Had Disease Thought to be of Such a Nature that it Would Recover Without Operation. Follow-up Results of Many of These Patients are Incomplete*

Site of Lesion	Bony or Stable Fibrous Ankylosis	Unstable Fibrous Ankylosis
Lumbo-sacral	3	—
Lumbar	58	1
Thoraco-lumbar	10	2
Mid and lower thoracic	21	4
Upper thoracic	1	1
Cervical	4	—
	97	8

No. of relapses at site of original lesion 8
,, ,, ,, another site or organ 3

TABLE VI.—*Classification According to Types of Reactivation of 21 Patients Readmitted for Further Treatment*

Readmitted for operation on fresh lesion in spine	2
,, ,, further operation on lesion treated previously by operation	8
Readmitted for disease elsewhere, renal or skeletal	4
Readmission for posterior spinal fusion	3
Readmitted for additional constitutional and antibiotic treatment	3
Died elsewhere of tuberculous meningitis	1

All these patients, except one who died and one still under treatment, have made a full recovery.

a child who had been treated by direct operation late in the disease, and the other a West Indian with extensive disease extending over nine vertebral bodies. These 21 patients have since readmission recovered and maintained their recovery with the exception of the West Indian, who is completing his treatment. Only one patient in the operative series has died of tuberculosis—a woman who was reported to have developed tuberculous meningitis three years after her discharge from Black Notley. Another patient died of non-specific pneumonia three years after discharge. The mortality rate of less than 2% for this disease on follow-up compares very favourably with the mortality rate before the introduction of antibiotics, which for most centres on five-year follow-up was approximately 30%.

The results obtained by constitutional therapy, antibiotics, and direct operation on the lesion are very reassuring, and patients have been allowed to return to full activities soon after leaving hospital. Children have been permitted to return to ordinary school and to take part in games within a short time. A spinal brace is worn by some patients on discharge, but seldom for longer than four months. A summary of the occupations to which operated patients have returned is shown in Table VII.

TABLE VII.—*Particulars Concerning Employment of 120 Patients Treated by Direct Operation for Vertebral Tuberculosis*

Children (16)			
Pre-school age	2	Attending special school	4
Attending ordinary school	10		
Adults: Full Employment (86)			
Household duties	33	Ship's fireman	1
Engineering	14	Lorry driver	1
Office	18	Dock labourer	1
Salesman	2	Butcher	1
Carpenter	2	Sailor	1
Teaching	4	Various	7
Porter	1		
Adults: Employed Part-time (9)			
Household duties	5	Various	4
Adults: Not Employed (9)			
In mental hospital	4	Unemployed	4
Paralysis due to stroke	1		

The average duration of treatment of the patients treated by direct operation was 9.7 months. These figures show that, by the direct operative treatment of tuberculosis of the spine, good and relatively speedy results can be obtained, with the early return of the patient to full employment. With a two-rib costotransversectomy approach the operation is safe if done with precision and deliberation, with the aid of preliminary constitutional and antibiotic therapy, and with a sufficient antibiotic cover. By this route an adequate access can be obtained to two or three vertebral bodies. For more extensive lesions the transpleural route advocated by Hodgson and Stock (1956) may well be preferable if facilities are available for its safe performance. After the debridement of the vertebral lesion, whatever may be the route of access, the vertebral defect may be reinforced with cancellous bone chips taken from the posterior part of the iliac crest, though in the smaller lesions this procedure is not strictly necessary. If the transpleural approach has been used, an anterior strut graft may be inserted by the technique of Hodgson and Stock, and by preventing the onset of deformity this may be of great benefit to patients with an extensive lesion.

Summary

The results are given of a combination of constitutional treatment, antibiotics, and direct operation for the treatment of certain patients suffering from tuberculosis of the spine. The selection of suitable cases for this form of operative treatment depends, *inter alia*, on the situation of the vertebral lesion. Previous experience had shown that the prognosis was worse for tuberculosis of the lower thoracic spine than for disease in the lumbar region. Experience with the direct operation has been most encouraging; the recovery rate is more rapid and certain, and the return of function is assured in most patients. On the other hand, patients with disease in the lumbar region not operated on also did well. Tuberculosis of the spine can now be rendered a curable disease with a good prognosis.

I am grateful to Sir Heneage Ogilvie, Mr. S. L. Higgs, and Mr. Ronald Reid for their help in this work. I am indebted to Dr. Jack Dixon, whose skilled anaesthesia has made the operation safe, and to Dr. Franklin Wood, whose early interest in the possibilities of bone tomography contributed materially to the success of the operations. I also thank the Editor of the *Annals of the Royal College of Surgeons of England* for permission to use Table I.

REFERENCES

Butler, R. W. (1935). *Brit. J. Surg.*, **22**, 738.
Dobson, J. (1951). *J. Bone Jt Surg.*, **33B**, 517.
Griffiths, D. Ll., Seddon, H. J., and Roaf, R. (1956). *Pott's Paraplegia*. Oxford Univ. Press, London.
Hodgson, A. R., and Stock, F. E. (1956). *Brit. J. Surg.*, **44**, 266.
Swett, P. P., Bennett, G. E., and Street, D. M. (1940). *J. Bone Jt Surg.*, **22**, 878.

STANLEYVILLE I AND II

TWO NEW VARIANTS OF ADULT HAEMOGLOBIN

BY

PAULETTE DHERTE
Belgian Congo Provincial Medical Laboratory, Stanleyville, Belgian Congo

J. VANDEPITTE, M.D.
Department of Bacteriology, Lovanium University, Leopoldville, Belgian Congo

J. A. M. AGER, M.B., B.S.
Department of Pathology, St. Thomas's Hospital, London

AND

H. LEHMANN, M.D., Sc.D., M.R.C.P., F.R.I.C.
Department of Pathology, St. Bartholomew's Hospital, London

In the course of a survey of haemoglobin types seen in the antenatal clinic at Stanleyville, a number of women were discovered whose red cells did not sickle but whose haemoglobin behaved on electrophoresis and chromatography like a mixture of haemoglobins A and S—that is, the abnormal haemoglobin was haemoglobin D. This was confirmed by solubility tests after Itano (1953) where the solubility of the haemoglobin was that of AD samples and not of AS samples.

In addition two abnormal haemoglobins were found to resemble haemoglobin D in some respects but to differ in others.

Techniques Employed

Sickle-cell test	Daland and Castle (1948)
Paper electrophoresis	Hanging-strip method according to Lehmann and Smith (1954) Alkaline: barbitone buffer, *p*H 8.6 Acid: phosphate buffer, pH 6.5
Alkali denaturation	1-minute test of Singer, Chernoff, and Singer (1951)
Cold denaturation	Rigas, Koler, and Osgood (1956)
Solubility	Itano (1953)
Chromatography	Huisman and Prins (1955)

"Stanleyville I"

In one woman belonging to the Lugbara tribe paper electrophoresis at *p*H 8.6 demonstrated haemoglobin A and a haemoglobin variant amounting to 25% which moved slightly faster than haemoglobin S or D and resembled haemoglobin L or P by that method (Fig. 1). The red cells did not sickle. There was no foetal haemoglobin, and the haemoglobin mixture was highly soluble when tested according to Itano (1953): >5 g./l. in 2.24 M phosphate buffer, and 1.8 g./l. soluble in 2.58 M phosphate buffer. The abnormal haemoglobin was not resistant to alkali-denaturation but was resistant to cold-denaturation. Her husband and four of her five children showed haemoglobin A only, but one daughter aged 12 showed the same haemoglobin composition as her mother. Details regarding their blood are given in Table I. Whereas on paper electrophoresis at alkaline *p*H the abnormal haemoglobin resembled L or P, it could be distinguished clearly from these two by chromatography on amberlite resin at *p*H 6. By this technique haemoglobin P does not separate properly from haemoglobin A, haemoglobin D moves more slowly than A, and haemoglobin L moves more slowly still. The abnormal component in the blood of the propositus and her daughter moved between L and P.

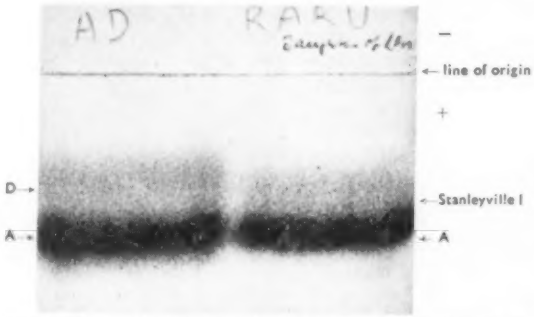


FIG. 1.—Comparison by hanging-strip paper electrophoresis at *p*H 8.6 of haemoglobin A plus D and A plus Stanleyville I. The new haemoglobin moves faster than haemoglobin D and more slowly than haemoglobin A; its position resembles that in which L and P would be found.

TABLE I.—*Red Cells in Carriers of Haemoglobin Stanleyville I*

	Count c.mm.	Hb/100 ml.	P.C.V. %	M.C.V. μ^3	M.C.H. $\mu\mu$g.	M.C.H.C. %	Appearance of Film
Propositus ..	4,180,000	12·5	39·5	95	30	32	Normal
12-year-old daughter ..	4,200,000	12·4	40	96	30	32	,,

A mixture of haemoglobins A, P, L, and of the abnormal variant separated into three fractions in the following order: A+P, the abnormal haemoglobin, and L (Fig. 2). On the other hand, a mixture of haemoglobins A+S or A+D and the haemoglobin of the propositus separated into two fractions only, one with the mobility of haemoglobin A and one with that of haemoglobin S or D (Fig. 3). This hitherto undescribed haemoglobin variant, which on paper electrophoresis at alkaline *p*H behaves like haemoglobin L or P, but which on chromatography at *p*H 6 behaves like haemoglobin S or D, is named, provisionally, haemoglobin "Stanleyville I."

The propositus was a Lugbara, and her family all live in the Aru territory in the extreme north-east of the Belgian Congo. The Lugbara are Nilotes, and the haemoglobin described as D by Vandepitte in 1956, which, however, moved, as the illustrations show, somewhat faster than D on alkaline electrophoresis, was found in four members of a family belonging to the Lago tribe, who are Nilotes from the same part of the Belgian Congo.

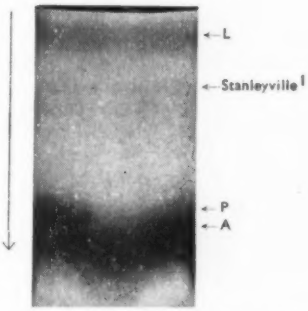


FIG. 2.—Results of ion-exchange chromatography of a mixture of haemoglobins A plus Stanleyville I, A plus P, and A plus L. Haemoglobin P does not separate from A, while Stanleyville I and L separate from A and from each other.

"Stanleyville II"

Another haemoglobin resembling haemoglobin D has been seen in two unrelated families. The first propositus belonged to the Budu tribe. Her husband and four of her five surviving children showed haemoglobin A only, but one child—a daughter aged 6 years—showed the same haemoglobin composition as her mother. The Budu are considered Bantu; they live in the north-east of the Belgian Congo and are surrounded by Nilotic tribes. The other propositus was not discovered in the course of the survey of pregnant women, but was a boy aged 8 who was admitted to hospital for albuminuria. Subsequently his mother was found to show the same haemoglobin composition as her son. She came from the River Uele region in the north-east of the Congo, where the population is of mixed Bantu-Nilotic origin. She was of mixed Greek-African origin.

The blood of these four individuals did not sickle and there was no foetal haemoglobin present. Table II shows details regarding their red cells. The abnormal haemoglobin was not resistant to alkali-denaturation but was resistant to cold-denaturation. On electrophoresis at alkaline *p*H on paper and starch, haemoglobin A was found, and also a second fraction which was

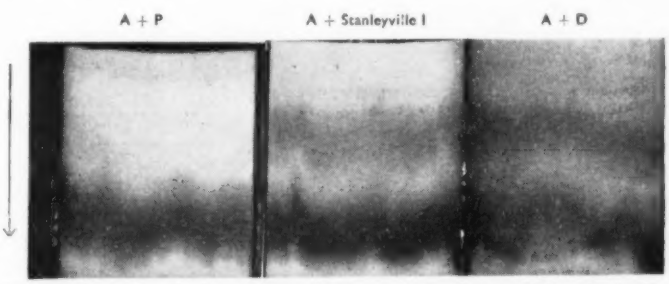


FIG. 3.—Comparison by ion-exchange chromatography of haemoglobins A plus P, A plus Stanleyville I, and A plus D. Although on paper electrophoresis at alkaline *p*H Stanleyville I moves faster than D and resembles P (Fig. 1), on chromatography it has the mobility of D.

TABLE II.—*Red Cells in Carriers of Haemoglobin Stanleyville II*

	Count c.mm.	Hb/100 ml.	P.C.V. %	M.C.V. μ^3	M.C.H. $\mu\mu$g.	M.C.H.C. %	Appearance of Film
1st propositus ..	3,450,000	10·0	32	93	29	31	Normal
1st propositus's 6-year-old daughter ..	4,200,000	13·1	40	96	31	33	,,
2nd propositus ..	3,880,000	10·3	34	88	27	30	,,
2nd propositus's mother ..	4,400,000	13·0	43·5	99	30	30	,,

indistinguishable from haemoglobin S or D by this technique (Fig. 4). On paper electrophoresis at acid *p*H no separation from A was achieved. However, on chromatography on amberlite resin at *p*H 6 two fractions were seen, one moving like haemoglobin A and one moving behind haemoglobin S or D but faster than haemoglobin L.

Mixtures of this haemoglobin with haemoglobins A, S, and L formed four distinct bands (Fig. 5). The solubility of the haemoglobin of the first propositus, which consisted of 40% of this hitherto undescribed variant and 60% of haemoglobin A, was rather low: measured according to Itano (1953) it was 1.1 g./l. of 2.58 M phosphate buffer. The haemoglobin of the first and of the second propositus and that of the son of the second propositus were all fully soluble in 2.24 M phosphate buffer in the test according to Itano. The haemoglobin of the daughter of the first propositus could not be tested for solubility. The haemoglobin variant described here, which on paper electrophoresis at *p*H 8.6 behaves like haemoglobins S or D, but which on chromatography at *p*H 6 differs from both by moving between haemoglobins S or D and L, we propose to name, provisionally, haemoglobin "Stanleyville II."

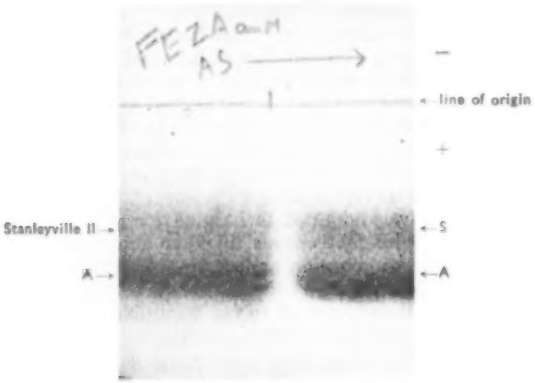


FIG. 4.—Comparison by hanging-strip paper electrophoresis at *p*H 8.6 of haemoglobin A plus S and A plus Stanleyville II. Haemoglobin Stanleyville II has the mobility of S or D.

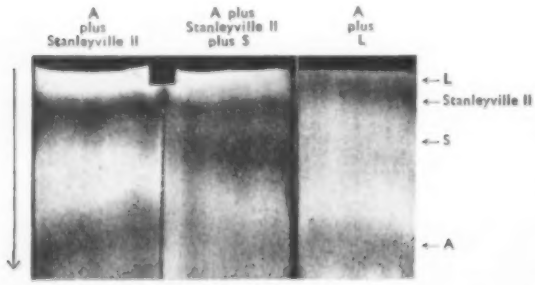


FIG. 5.—Comparison by ion-exchange chromatography of haemoglobin A plus Stanleyville II, a mixture of A plus Stanleyville II plus S, and of A plus L. Although on paper electrophoresis at alkaline *p*H Stanleyville II moves like S or D (Fig. 4), on chromatography it moves more slowly than S or D but not so slow as L.

Summary

Two hitherto unrecorded familial variants of adult haemoglobin are described. One, "Stanleyville I," was found in a Lugbara (Nilotic) family and is thought to be identical with one previously described when it was thought to be D, also occurring in a Nilotic family. The second, "Stanleyville II," was seen in two families, one belonging to the Budu tribe—a Bantu community surrounded by Nilotes—the other being of mixed Greek-Bantu-Nilotic origin.

REFERENCES

Daland, G. A., and Castle, W. B. (1948). *J. Lab. clin. Med.*, **33**, 1082.
Huisman, T. H. J., and Prins, H. K. (1955). Ibid., **46**, 255.
Itano, H. (1953). *Arch. Biochem.*, **47**, 148.
Lehmann, H., and Smith, E. B. (1954). *Trans. roy. Soc. trop. Med. Hyg.*, **48**, 12.
Rigas, D. A., Koler, R. D., and Osgood, E. E. (1956). *J. Lab. clin. Med.*, **47**, 51.
Singer, K., Chernoff, A. I., and Singer, L. (1951). *Blood*, **6**, 413.
Vandepitte, J. (1956). *Bull. Acad. roy. Sci. colon.*, **2**, 697.

Those recently appointed to, or promoted in, the Venerable Order of the Hospital of St. John of Jerusalem include the following members of the medical profession:

As Knights: Surgeon Vice-Admiral Sir R. C. MAY, K.B.E., C.B., *M.C.*, Colonel J. J. ABRAHAM, C.B.E., D.S.O., and Dr. G. D. W. CAMERON. *As Associate Knight:* Dr. G. L. KIRK. *As Commanders (Brothers):* Surgeon Rear-Admiral W. R. S. PANCKRIDGE, Q.H.P., Messrs. J. C. N. WAKELEY, W. H. C. ROMANIS, *M.C.*, and R. A. H. FULTON, and Drs. W. H. SHILVOCK, E. H. EASTCOTT, L. M. MAYBURY, C. HOMI, J. BROWN, T. E. WOOD, H. R. WYNNE, W. K. HAY, J. M. RUSSELL, T. T. BAIRD, R. V. C. RICHARDS, D. C. BEWS, L. J. CALVERT. *As Associate Commander (Brother):* Mr. D. VAIL. *As Commander (Sister):* Dr. ELLEN W. M. SHAW. *As Officers (Brothers):* Surgeon Captain B. S. LEWIS, D.S.C., and Surgeon Commodore T. B. McLEAN, Brigadiers P. TREMBLEY, O.B.E., and G. A. SINCLAIR, O.B.E., Temporary Colonel T. A. PACE, O.B.E., and Major J. LAPPER, and Drs. G. GILLIES, N. V. M. DODDS, Z. G. PANOS, E. M. CLARK, A. P. BROWN, P. ALWYN-SMITH, I. R. S. ROBERTSON, H. MacG. SINCLAIR, I. A. BALMER, W. W. BELL, J. E. HILTZ, H. C. POWELL, R. C. WILSON, K. C. CHARRON, and P. VAUGHAN. *As Officer (Sister):* Dr. LUCIE L. VAN DAM. *As Serving Brothers:* Colonel O. G. PROSSER, T.D., Wing Commander W. J. S. KETTLES, and Drs. A. J. K. WILSON, A. E. AINSCOW, C. LEITH-BARRON, C. J. DE VERE SHORTT, H. S. KENT, T.D., W. L. LISTER, A. FOWLER, L. WILKIE, E. D. CLIFFORD-JONES, J. D. JONES, J. PATERSON, J. D. O'M. POOLE, J. W. P. SALT, C. H. B. LAWFIELD, J. P. BUSH, A. T. H. GLANVILL, H. R. A. MICHELMORE, J. W. PIPER, J. B. LEE, C. E. PEARSONS, D. M. ROSS, D. H. F. MILMO, R. H. P. FERNANDEZ, D. A. IRELAND, W. H. HYLTON, J. M. NORMAN, K. N. MAWSON, G. S. MORGAN, M. R. EL SARRAFF, H. E. M. WILLIAMS, and J. J. M. G. GRAVEL. *As Associate Serving Brothers:* Drs. J. LEVY, S. LONG, I. FRACK, S. CAMINETSKY. *As Serving Sisters:* Drs. MARGARET F. GILLISON, KATHLEEN A. WILSON, BARBARA R. A. DEMAINE, MARIAN I. TEMPLIN, and ELIZABETH H. B. YOUNG.

A NEW HAEMOGLOBIN VARIANT IN AN AMERICAN NEGRO*

BY

ROSE G. SCHNEIDER, Ph.D.

Tissue Metabolism Research Laboratory, University of Texas Medical Branch, Galveston, Texas

AND

MARY ELLEN HAGGARD, M.D.

Department of Paediatrics, University of Texas Medical Branch, Galveston, Texas

In the course of a survey of the incidence of abnormal types of haemoglobin a sample was obtained from J.D., a negro male, who had been admitted to the hospital with a diagnosis of benign prostatic hypertrophy. On clinical and haematological examination of this patient no symptoms referable to anaemia or haemolysis were found nor could sickling of the erythrocytes be elicited.

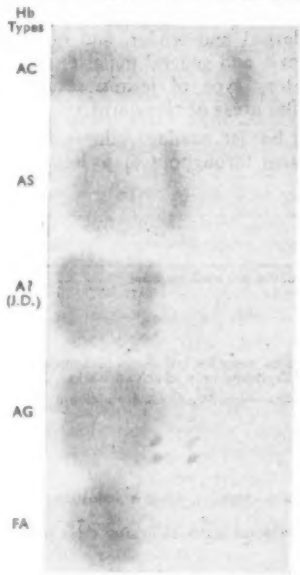


FIG. 1. — Paper electrophoresis pattern of J.D.'s haemoglobin sample compared with others. Veronal buffer *p*H 8.6, ionic strength 0.05.

His haemoglobin sample analysed by paper electrophoresis, veronal buffer *p*H 8.6, separated into two approximately equal fractions, one of which was indistinguishable from haemoglobin A; the mobility of the other fraction was like that of haemoglobin L (Ager and Lehmann, 1957) or P (Schneider and Haggard, 1958)—that is, between haemoglobin types G and S (or D) (Fig. 1). Similar results were obtained with starch-block or starch-gel electrophoresis, at *p*H 8.6 (the former in veronal buffer, the latter in tris-EDTA-borate buffer).

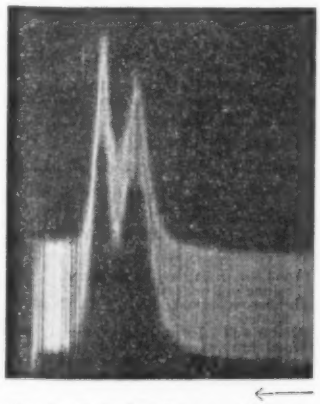


FIG. 2.—Scanning diagram of haemoglobin of J.D. Ascending pattern 1% carboxyhaemoglobin, cacodylate buffer *p*H 6.5, ionic strength 0.1.

In moving boundary electrophoresis, cacodylate buffer *p*H 6.5, ionic strength 0.1, J.D.'s haemoglobin sample resolved into two approximately equal peaks, corresponding in mobility to types S (or D) and A, respectively (Fig. 2). When an aliquot of haemoglobin S was added to J.D.'s sample and the mixture analysed in moving boundary electrophoresis, cacodylate buffer *p*H 6.5, the leading peak was increased in proportion to the amount of added S. In column chromatography with the ion-exchange resin "amberlite IRC-50," citrate buffer *p*H 6 (Huisman and Prins, 1955), J.D.'s haemoglobin sample again developed into two components, corresponding to types A and S (or D), respectively (Fig. 3). These results with the methods of free electrophoresis and ion-exchange chromatography, both with acid buffers, serve to differentiate the variant in J.D. from haemoglobins L and P, the two types it resembles in zone electrophoresis in alkaline buffers. In ion-exchange chromatography, citrate buffer *p*H 6, the mobility of L is distinctly less than that of S or D, while that of P is distinctly greater; in fact, in this method P does not separate well from haemoglobin A. In moving boundary electrophoresis, cacodylate buffer *p*H 6.5, P appears identical with A. No appreciable amounts of foetal haemoglobin or of haemoglobin A_2 could be detected in J.D.'s sample. No other members of his family were available for examination.

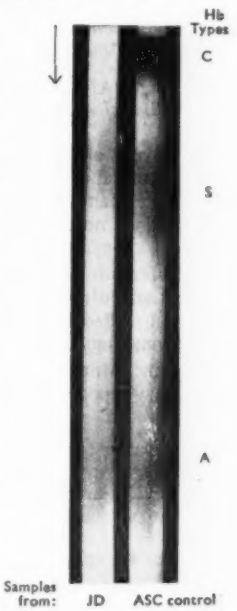


FIG. 3. — Chromatography of haemoglobin of J.D., "amberlite IRC-50," citrate buffer *p*H 6.

We have communicated our findings to Dr. H. Lehmann, who kindly informed us that a variant with similar or identical properties has recently been found by Dherte, Vandepitte, Ager, and Lehmann (1959), and designated Stanleyville I. A comparison in London of the present haemoglobin and of Stanleyville I found the two to be indistinguishable. Therefore, at present we shall not propose a separate designation for the variant under discussion.

*This research was supported by a grant from the U.S. Public Health Service.

REFERENCES

Ager, J. A. M., and Lehmann, H. (1957). *Brit. med. J.*, **2**, 142.

Dherte, P., Vandepitte, J., Ager, J. A. M., and Lehmann, H. (1959). Ibid., **2**,

Huisman, T. H. J., and Prins, H. K. (1955). *J. Lab. clin. Med.*, **46**, 255.

Schneider, R. G., and Haggard, M. E. (1958). *Nature (Lond.)*, **182**, 322.

The Ross Clinic, a regional treatment unit providing diagnostic and treatment facilities of the most up-to-date kind, has been opened in the grounds of the Royal Mental Hospital, Aberdeen. The Professor and staff of the University Department of Mental Health have their clinical, teaching, and research facilities in this unit. There is a 40-bed in-patient department for the intensive treatment of early and mild psychotic reactions, psychoneurosis, and psychosomatic disorders, day-hospital facilities for some 20–30 patients, and an extensive out-patient department. There are also beds available for the admission of acute cases for short periods of observation.

GRISEOFULVIN TREATMENT OF ACUTE CATTLE RINGWORM INFECTIONS IN MAN

BY

THOMAS COCHRANE, M.D., F.R.F.P.S.
Consultant Dermatologist, Ayr County Area

AND

ADAM TULLETT, M.B., Ch.B.
Clinical Assistant, Heathfield Hospital, Ayr

The discovery of an efficient systemic antibiotic for use against acute and chronic fungus infections of the skin has long been awaited by dermatologists. With griseofulvin it now seems to be at hand.

Gentles (1958) reported the successful oral treatment of trichophyton and microsporon infections in guinea-pigs with griseofulvin, and Lauder and O'Sullivan (1958) found it effective in calves with *Trichophyton verrucosum* ringworm.

Williams, Marten, and Sarkany (1958) published a preliminary report of the use of griseofulvin in nine cases of *Trichophyton rubrum* infection and one case of *Microsporon audouini* infection of the scalp. They considered that the results supported the hope that griseofulvin might be of therapeutic value.

During the first three months of 1959 this antibiotic has been used to treat fungus infections in the skin clinics in Ayrshire. As this is an agricultural area the incidence of acute cattle ringworm infections of the skin is high. This short paper has been prompted by the very encouraging results of treatment with griseofulvin in these cases.

The results of treatment in 16 cases of acute inflammatory cattle ringworm are summarized in Table I. The acute inflammatory lesions were essentially kerions—nodular, boggy, exudative circumscribed tumours which were studded with pustules. Frequently the lesions were crusted and foul-smelling. The neighbouring lymphatic glands were enlarged and tender, and often the patient had a mild pyrexia and general malaise. In addition to this inflammatory type of lesion, several cases had acute active annular areas of ringworm.

In addition to a vesicular border, scaling, redness, and slight infiltration were present throughout these lesions,

TABLE I

Case No.	Age and Sex	Site	Clinical Type	Duration in Weeks	Daily Dose	Duration of Treatment	Time to Clinical Cure	Remarks
1	45 M	Beard	Kerions	2	2 g. 1 ,,	1 week 3 weeks	3 weeks	Culture 3rd week negative
2	32 F	Back of neck	Kerion	2	2 ,, 1·5 ,, 1 ,,	1 week 2 weeks	3 ,,	,, 4th ,, ,,
3	6 F	Nose, forehead	Annular	3	1 ,, 0·75 ,,	2 ,, 2 ,,	2 ,,	Scales negative on direct examination. Erythema only after two weeks
4	45 M	Beard	Kerions	3	2 ,, 1·5 ,, 1 ,,	1 week 1 ,, 2 weeks	3 ,,	Hairs—negative, direct examination
5	20 M	Beard, neck	,,	2	2 ,, 1·5 ,, 1 ,,	1 week 1 ,, 2 weeks	3 ,,	
6	42 M	Beard, right forearm	,,	4	2 ,, 1 ,,	1 week 3 weeks	2½ ,,	Hairs—negative, direct examination
7	26 F	Eyebrow, neck, cheek	Kerion, annular	2	1·5 ,, 1 ,,	10 days 3 weeks	3 ,, 2 ,,	Epidermal scales clear after three weeks
8	37 M	Neck	Kerions	2	1·5 ,, 1 ,,	1 week 3 weeks	2 ,,	
9	56 F	Neck, cheeks	Annular	3	1 ,,	3 ,,	12 days	No relapse three weeks after treatment stopped. Direct examination negative
10	34 F	Neck, cheeks, arms	,,	4	1·5 ,, 1 ,,	5 days 3 weeks	2 weeks	Scales—negative on direct examination after three weeks
11	16 M	Scalp, right forearm	Kerions	4	1 ,,	4 ,,	3 ,,	No relapse three weeks after treatment
12	25 M	Beard	,,	3	1 ,,	4 ,,	2–3 ,,	No relapse three weeks later. Hairs negative on direct examination
13	10 M	Scalp	,,	2	1 ,, 0·75 ,,	2 ,, 2 ,,	3 ,,	No recurrence. Hairs negative on direct examination
14	18 F	Chin, cheeks	Annular	4	1 ,,	3 ,,	12–15 days	Slight erythema, but direct examination negative after three weeks
15	12 F	Right palm and fingers	,,	8	1 ,,	4 ,,	2–3 weeks	Clinically normal skin after three weeks. Treatment continues
16	23 M	Beard, chest	Kerions, annular	2	1 ,,	3 ,,	2–3 ,,	Chest cleared in 12 days. Direct examination negative. Treatment continues

TABLE II

Case No.	Age and Sex	Site	Duration	Culture	Daily Dose	Duration of Treatment	Remarks
1	55 F	Finger-nails	20 years	*T. rubrum*	2 g. 1·5 ,, 1 ,,	2 weeks 2 ,, 6 ,,	Only distal 1/3 now affected. Treatment continues
2	8 M	Scalp	4 months	*T. schoenleini*	1 ,,	6 ,,	Wood light negative. Head shaved. 2nd culture 5th week negative
3	14 M	Right palm, nails	9 ,,	*T. rubrum*	2 ,, 1 ,,	4 ,, 4 ,,	Hands now normal. Distal 1/3 nails only affected
4	38 F	Finger-nails	3 years	,, ,,	1 ,,	8 ,,	Almost well. Treatment continues
5	9 M	Scalp	9 months	*M. audouini*	1 ,,	5 ,,	Wood light negative after three weeks. Head clipped
6	28 M	Left palm	2 years	*T. rubrum*	2 ,, 1 ,,	2 ,, 4 ,,	No irritation. Direct examination now negative. Treatment continues
7	30 M	Right ,,	5 ,,	,, ,,	1 ,,	6 ,,	No itch. Scaling now clear. Clinically cured
8	45 M	Feet	8 ,,	,, ,,	1 ,,	3 ,,	No irritation. No fresh vesicles three weeks after treatment
9	10 M	Scalp	6 months	Wood light positive. No culture	1 ,,	4 ,,	Scalp shaved after two weeks. Wood light negative

and there was little evidence of central clearing as is common in the classical tinea circinata. Occasionally superficial pustules were present in the centre of the lesions.

All of the 16 cases had been in contact with cattle or farm buildings, and in every case culture from hairs or epidermal scrapings produced *Trichophyton verrucosum*. At the start of this series an initial daily dose of 2 g. of griseofulvin was given for one week and then reduced as the clinical appearance of the lesion responded to treatment. In subsequent cases, however, treatment was started and continued with 1 g. daily—with little or no effect on the duration of clinical involution of the active lesions. No local treatment was used apart from 1/4,000 mercury perchloride lotion to the crusted and foul-smelling lesions and mechanical removal of all loose hairs in the area.

Routine blood examinations were done weekly on every patient, but no abnormality was detected. Liver-function tests were also carried out on several patients, but again these were normal.

Two patients complained of mild gastro-intestinal upset when taking 2 g. of the antibiotic daily, but this disappeared when the dose was reduced to 1 g. daily.

To compare the response to griseofulvin therapy four cases of cattle ringworm infection were kept on routine standard treatment. Three of these had acute inflammatory lesions of the beard and scalp and one had a widespread annular ringworm of the face, neck, and shoulders. Treatment consisted in removing loose hairs and using hot boric lint fomentations, antiseptic lotions, and fungicidal ointments. In the acute inflammatory cases treatment was continued for nine and ten weeks before resolution took place, while, in the case of annular ringworm, treatment was required for six weeks before fresh lesions ceased to appear. This has been our experience in the treatment of these cases over the past five years in Ayrshire.

The most noticeable difference, in our opinion, between the cases treated routinely and those treated with griseofulvin, apart from the duration of clinical involution, was the rapid disappearance of general malaise, pain, and discomfort in the cases treated with the antibiotic. In nearly all cases this had completely gone after one week of treatment. Another difference found was in the response of the early satellite lesions. In the griseofulvin-treated cases these did not develop further, as was the case in the routinely treated patients, but simply settled down with a rapid disappearance of all inflammatory signs.

In addition to these cases of acute cattle ringworm infections we have also started treatment of several other types of ringworm infections with griseofulvin. The results are summarized in Table II. In our opinion these results show that griseofulvin is an antibiotic of great value in the treatment of a large variety of fungus infections of the skin. It would appear to open up a new era in the treatment of human ringworm infection, and will banish for ever, we hope, the necessity to epilate a scalp or beard by *x* rays.

Comments

The new systemic antibiotic griseofulvin now seems to be the treatment of choice in acute cattle ringworm infections of the human skin.

A daily dose of 1 g. seems to be adequate at present. However, the minimum effective dose and the optimum dose of the drug have yet to be established. The duration of the infection does not seem to have any bearing on the response to treatment.

In acute inflammatory ringworm of the beard and scalp the duration of treatment has been shortened by approximately six weeks. The pain and discomfort in the lesions and the general toxicity of the patient clear much more rapidly with griseofulvin. The duration of treatment will depend on the type of infection and tissue involved.

In the present series of cases, only mild side-effects were seen in two patients. In prolonged treatment, however, as, for example, in tinea of the nails, routine blood examination is still thought advisable, although it would seem to be unnecessary when the antibiotic is given only for short periods.

We are indebted to the staff of the department of medical mycology, University of Glasgow, for their considerable help in supplying the culture reports in this series of cases. The griseofulvin used in this series was supplied by Glaxo Laboratories Ltd.

REFERENCES

Gentles, J. C. (1958). *Nature (Lond.)*, **182**, 476.
Lauder, I. M., and O'Sullivan, J. G. (1958). *Vet. Rec.*, **70**, 949.
Williams, D. I., Marten, R. H., and Sarkany, I. (1958). ***Lancet***, **2**, 1212.

Medical Memoranda

Calcified Subphrenic Abscess

Amoebic abscesses of the liver are fairly common in Singapore, and usually present with pain and tenderness over the right lower chest or hypochondrium, fever, and leucocytosis. The case reported here was diagnosed and treated as an amoebic liver abscess, the unusual feature being the massive calcification of the abscess. An almost identical radiological finding was reported by Bruce (1957) in a young Englishman who was symptomless but gave a past history of amoebic dysentery. Bruce concluded that his patient had a calcified amoebic liver abscess, but, because there were no symptoms, did not treat him. Necropsy of the present case, however, showed that the calcified abscess was in fact subphrenic and not in the liver.

CASE REPORT

A male Chinese cook aged 57 was admitted to the General Hospital, Singapore, with a five-days history of continuous pain in the right hypochondrium, aggravated by pressure and occasionally radiating to his right back and right shoulder; this was associated with anorexia, loss of weight, and mild fever. He had no cough, jaundice, or recent diarrhoea. He remembered having had similar pain in China at the age of 17 years, following an attack of diarrhoea, and eventually recovering without medical treatment.

On examination he was pale, thin, and wasted, with a temperature of 100.4° F. (38° C.); he was not jaundiced. The right lower chest was bulging anteriorly and laterally, and there was tenderness over the intercostal spaces in this

area. Air entry was good over both lungs, but few crepitations were heard over the right base. The right upper quadrant of the abdomen was distended, with guarding and tenderness over the right subcostal area. Neither liver nor spleen was palpable. There was no free fluid in the abdomen or any abnormality on rectal examination.

Investigations.—Haemoglobin, 8.4 g./100 ml.; W.B.C., 12,600/c.mm. (neutrophils 88%); E.S.R. 85 mm. (Westergren). Stools contained no *Entamoeba histolytica* cysts or trophozoites. An *x*-ray film of his chest showed moderate pulmonary emphysema with old tuberculous scarring at the right apex, increased pulmonary markings at the right base, and a calcified shadow under the right diaphragm. Further *x*-ray films and fluoroscopy revealed a massive oval calcified shadow measuring 16 by 12 by 10 cm. under the right diaphragm with mottled calcification in the periphery and a small fluid level in the upper portion (Fig. 1); the right diaphragm was moderately elevated.

It was concluded that the patient probably had a liver abscess with calcification in its wall, and, since most liver abscesses seen in Singapore are amoebic in origin, he was given a course of emetine and tetracycline followed by chloroquine. There was no clinical improvement, and an initial aspiration of the abscess produced 750 ml. of thick greenish sterile pus. A plain *x*-ray film of the abdomen then showed partial collapse of the medial wall of the abscess (Fig. 2). The patient's general condition improved, and after further aspirations of large amounts of pus he was discharged. Three months later he was readmitted with similar pain, and after more antibiotic and anti-amoebic therapy with further aspirations he again improved and was discharged. Two months later he was admitted a third time, and was given yet another course of anti-amoebic treatment and tetracycline in conjunction with aspirations. This time he did not recover. The calcified shadow had persisted since his first admission, partially collapsing with each aspiration but regaining its original rounded shape as it refilled again with pus.

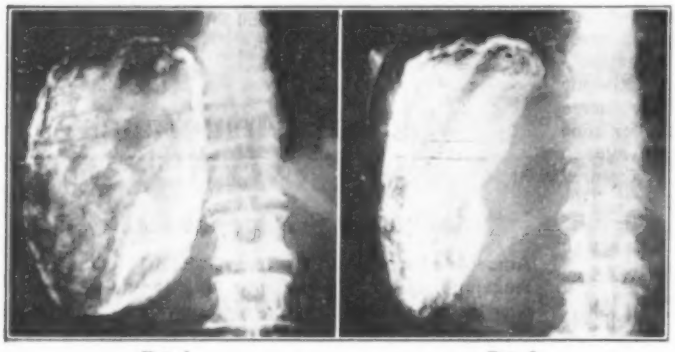


FIG. 1 FIG. 2

FIG. 1.—Postero-anterior radiograph of the abscess. FIG. 2.—The abscess after aspiration, showing collapse of medial wall.

At necropsy a large abscess (18 by 10 cm.) with a hard calcified wall 1.5–3 cm. thick was found immediately below the right leaf of the diaphragm, pushing the liver downwards and medially (Fig. 3). The diaphragmatic surface of the lower lobe of the right lung was bound down to the right leaf of the diaphragm, which could not be defined clearly, as it merged into the superior wall of the calcified abscess. The inferior wall of the abscess was adherent to the superior surface of the right lobe of the liver, which itself was normal. It was possible to open the abscess only by sawing through it. A small quantity of thick greyish pus, which was sterile on culture, filled the abscess cavity. Smears and culture did not reveal any *E. histolytica*. The gall-bladder and gastro-intestinal tract were normal.

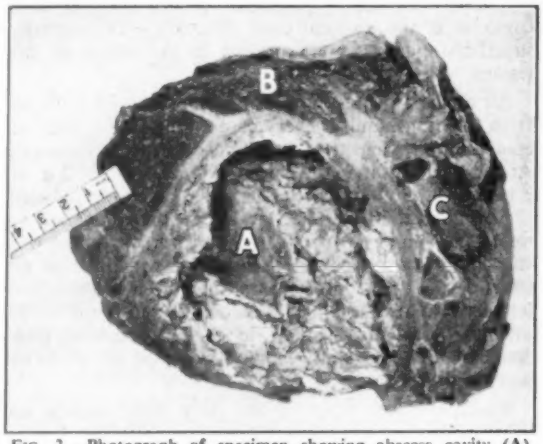


FIG. 3.—Photograph of specimen showing abscess cavity (A), lung above (B), and ribs (C).

COMMENT

The remarkable feature in this case was the massive calcification which obviously prevented complete collapse of the abscess wall and occlusion of the cavity after each aspiration. In view of the calcification it is probable that the abscess had been present for a very long time and did not give rise to any symptoms except for a few days before his admission. That a subphrenic abscess can remain quiescent is not altogether unknown. Russell (1929) and Janz (1933) each reported a case in which the condition remained unrecognized for seven years after its onset. Lockwood (1921) and Grove (1930) have remarked on the occasional existence of subphrenic abscess with relatively few or no symptoms. There are only a few reports on calcification of subphrenic abscess—that by Freese in 1935, and the one by Bruce (1957) which on the basis of this case report was probably a subphrenic abscess. It is interesting to note that when Ochsner and DeBakey (1938) reviewed 3,608 cases of subphrenic abscess they did not mention seeing a calcified abscess.

ANDREW CHEW GUAN KHUAN, M.B., B.S.,
Medical Officer, General Hospital, Singapore.

REFERENCES

Bruce, R. (1957). *Brit. med. J.*, **1**, 1343.
Freese, K. (1935). *Röntgenpraxis*, **7**, 368.
Grove, L. (1930). *Trans. sth. surg. Ass.*, **42**, 15.
Janz, G. (1933). *Arch. klin. Chir.*, **178**, 482.
Lockwood, A. L. (1921). *Surg. Gynec. Obstet.*, **33**, 502.
Ochsner, A., and DeBakey, M. (1938). *Int. Abstr. Surg.*, **66**, 426.
Russell, T. H. (1929). *Ann. Surg.*, **90**, 238.

The latest edition of the *Directory of Contributory Scheme Benefits* (price 10s., post free), and the second edition of the *Directory of Convalescent Homes in the Provinces* (price 5s., post free) are now available, and can be obtained from the British Hospital Contributory Schemes Association at Royal London Buildings, 142, Baldwin Street, Bristol, 1.

Reviews

BLOOD GROUPS

British Medical Bulletin. Volume 15, Number 2. *Blood Groups.* (Pp. 89–174; illustrated. 20s.) London: Medical Department, British Council. 1959.

The *British Medical Bulletin* must be regarded as one of the British Council's major achievements. It has a flair for picking just the right team of contributors to describe the recent advances and the present state of knowledge in one of the developing fields of medicine, particularly those to which British scientists have made a special contribution. The current number on blood groups is a good example of these virtues. It contains 15 articles by 19 authors presided over by A. E. Mourant. The reviewer of such a volume would wish to have the ability of a Lord Macaulay, so vast is the field. Up to now 59 antigens have been recognized in the red cells, grouped in eleven separate genetic systems. Their relative clinical importance, the value of the antiglobulin reaction or Coombs test in their recognition, and the pathology and management of haemolytic disease are fully discussed, but more than half the volume is devoted to the wider scientific implications of the blood groups.

Practically all the antigens are inherited as simple dominant characters, and their study has made an enormous contribution to knowledge of human inheritance. The survival of different members of a blood-group system when one might have been expected to fight its way to the top raises the same problems as the survival of common hereditary diseases such as sickle-cell anaemia and dementia praecox, which evolution should have eliminated unless they carried some compensating advantage to the race. This so-called *polymorphism* is being energetically examined. Blood groups also help us in classifying the races of mankind and tracing some of their recent migrations. Blood groups akin to those of man occur in animals, and haemagglutinins can be obtained from the seeds of plants. The fundamental role of these substances still remains obscure and research in this field is therefore an exciting venture.

Like any serious essay in human genetics this volume is not easy reading, but the writers and the editor are to be congratulated on a clear exposition of a difficult but important subject.

L. J. WITTS.

CELL AND TISSUE CULTURE

Cell and Tissue Culture. By John Paul, M.B., Ch.B., Ph.D., M.R.C.P.Ed. (Pp. 261+viii; illustrated. 30s.) Edinburgh, London: E. and S. Livingstone Ltd. 1959.

I greatly enjoyed reading this little book. Its style is easy and attractive and it certainly achieves what it sets out to do, for I felt, when I had finished it, that I could make a shot at culturing cells and tissues with reasonable success.

After outlining the early history of tissue culture and its emergence as a science, the author briefly summarizes the essentials of cell and tissue structure and function; some of the applications for pathology are stated and then the reader is launched upon the intricacies of growing things under artificial conditions. Dr. Paul certainly achieves great success in these sections, for he leads the inquirer on by simple stages over one obstacle after another until the final triumph is reached. I could almost hear him saying, "Well done!" at the end of the final exercise and feel his friendly pat on the back.

So far as I can tell, the book contains just about enough of general theory for an everyday manual. Much care has been given to the selection of a few well-proved methods of media preparation, staining, and the like, and the illustrations are clear and simple. Plenty of references are provided at the end of each chapter, yet it was here that I experienced a little disappointment. So many of these papers require more than a beginner's knowledge of cytology. It would be most useful in future editions to indicate by an asterisk or the use of Clarendon type those that could be tackled at once or that provide key knowledge to the subject under discussion. And I would also like to suggest that a good book on tumours, such as that by Professor R. A. Willis, be recommended. Incidentally, the only slip I could find was on page 20, where muscle tumours are said to be rare. This, of course, is not correct, since new growths of smooth muscle, especially in the uterus, are very common.

The publishers are to be congratulated on a neat, handy volume, and the index is reasonably comprehensive. The price, however, is a bit steep.

ROY CAMERON.

MEDICAL MYCOLOGY

Mycologie Médicale. Communications et Rapports Présentés aux Journées de Mycologie Médicale (14–15 Decembre, 1956). Organized by the Institut Pasteur and the Société Française de Mycologie Médicale. (Pp. 344; illustrated. 3,000 fr.) Paris: L'Expansion Scientifique Française. 1958.

This well-produced volume contains the papers given at a symposium on medical mycology which took place at the Pasteur Institute. They deal only with selected aspects, but the growing importance of mycology in general medicine is shown by the first two sections devoted respectively to pulmonary aspergillosis and cerebral mycosis. The third is devoted to Candida infections, which have increased in incidence following antibiotic therapy and have been diagnosed more frequently since the introduction of nystatin has provided a therapeutic test. There are exhaustive accounts of infection in infants by Candida, of its laboratory appearance, and other aspects, including the possible predisposing influence of "malignant haemopathies." The fourth section deals chiefly with the incidence of dermatomycoses in various French territories, and the fifth with tropical fungi. The last chapter contains a comprehensive list of antifungal agents, including many which are largely of theoretical interest; it was written before the introduction of griseofulvin. This is an authoritative book especially on candidiasis, and has a full bibliography and some excellent coloured pictures. General physicians and dermatologists will find much of interest in it, and a copy should be available in all mycology laboratories.

F. F. HELLIER.

THE RECOVERY ROOM

The Recovery Room. A Symposium. By John Adriani, M.D., and John B. Parmley, M.D. (Pp. 123+xii; illustrated. 32s. 6d.) Oxford: Blackwell Scientific Publications. 1959.

The recovery room is still a somewhat rare facility in the British hospital. The reason is partly because our hospitals are old, and partly because, with the large ward as the common nursing unit, the standard of nursing during the post-operative period is generally higher than is equally economically attainable in, say, single or double rooms. The term "recovery room" is capable of many interpretations. There is little doubt that

confusion exists in Britain as to what it does mean, and this has led hospitals to provide rooms which have not been as useful as they had hoped. Rooms intended for post-operative treatment of some days' duration are contiguous to an operating suite empty for a large part of each 24 hours. Such rooms may be without such elementary nursing facilities as a bed-pan unit or the means of making a cup of tea. In other hospitals an area intended for an hour or two's stay is situated some distance away from the operating team and where facilities for observation and emergency resuscitation are rudimentary.

The real purpose of these rooms, and hence their staffing needs both nursing and medical, and the necessary facilities and equipment which must be provided, are still matters which arouse intense discussion in interested circles. Considerable light is thrown on these and every other aspect of this problem by this little book. Here some 45 knowledgeable people in the United States give brief but pointed and often detailed answers to a host of questions about recovery rooms. Though these answers must be viewed against the background of American hospital practice, there is a great deal of valuable opinion for consideration by those in Great Britain interested in this problem. The book is strongly recommended.

W. W. MUSHIN.

IDEAS ON THE BRAIN

The History and Philosophy of Knowledge of the Brain and its Functions. An Anglo-American Symposium. London, July 15–17, 1957. Edited by F. N. L. Poynter, Ph.D., F.L.A. (Pp. 272+x; illustrated. 22s. 6d.) Oxford: Blackwell Scientific Publications. 1958.

This symposium was held in London as a historical introduction to the First International Congress of Neurological Sciences in July, 1957.

Hippocrates realized that the brain is an all-important organ. His view was supported by direct observation, and yet philosophers and physicians for the next 2,000 years often looked on the brain with little interest. In non-Western concepts, such as those of the Tibetan scrolls, the brain is entirely disregarded, as indeed are the lungs. The breathing exercises of Yoga practices are based on the idea that inhalation into a channel which spirals round the spine takes in the spiritual essence of immortal life. These and many other ancient concepts are of great interest, and yet how sad that we could not hear the views of, say, Aristotle or Descartes after they had become aware of what we now know of the function and structure of the brain.

The discoveries of the past century have of necessity changed man's conception of what goes on in his head. He now knows that his brain contains a universe of separate units whose remarkable qualities are at last being slowly unravelled, so that the separation of psychological from the physiological becomes more unreal with every year that passes.

In this symposium the last two papers describe the transformation resulting from modern knowledge: first a remarkable chapter by Dr. Mary Brazier on the evolution of concepts regarding electrical activity in the brain, 1600 to 1800; and second Dr. Chandler Brooks, with almost up-to-date accounts of excitation and inhibition, ion flux and membrane function, chemical transmission and the central synapse, and ideas regarding plasticity of the nervous system. Clearly there are going to be some exciting developments in knowledge of the central nervous system in the next few years.

W. RITCHIE RUSSELL.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

Children in Practice. By John Peterson. (Pp. 227+vii. 25s.) London: Cambridge University Press. 1959.

Wound Healing and Tissue Repair. Edited by W. Bradford Patterson. (Pp. 83+xi; illustrated. 21s.) Chicago: University of Chicago Press. London: Cambridge University Press. 1959.

Surgery for Nurses. By James Moroney, M.B., Ch.B., F.R.C.S.(Eng.), L.R.C.P.(Lond.). Sixth edition. (Pp. 751+xii; illustrated. 30s.) Edinburgh, London: E. and S. Livingstone Ltd. 1959.

Notable Names in Medicine and Surgery. By Hamilton Bailey, F.R.C.S.(Eng.), F.A.C.S., F.R.S.(Edin.), and W. J. Bishop, F.L.A. Third edition. (Pp. 216+xiii; illustrated. 35s.) London: H. K. Lewis and Co. Ltd. 1959.

A Synopsis of Anaesthesia. By J. Alfred Lee, M.R.C.S., L.R.C.P., M.M.S.A., F.F.A.R.C.S., D.A. Fourth edition. (Pp. 616; illustrated. 27s. 6d.) Bristol: John Wright and Sons Ltd. 1959.

A Pocket Book of Proprietary Drugs. Compiled by Alistair G. Cruikshank, F.R.C.P.E., and Cornelius Stewart, L.R.C.P.&S.E., M.P.S. (Pp. 236. 10s. 6d.) Edinburgh, London: E. and S. Livingstone Ltd. 1959.

Genetik des Menschen. Lehrbuch der Humangenetik. By Professor Otmar Freiherr von Verschuer, M.D. (Pp. 427+xi; illustrated. DM. 48.) Munich, Berlin: Urban and Schwarzenberg. 1959.

The Prescriber's List of Proprietary Medical Products. Alphabetically arranged. (Pp. 366. 15s.) London: The Unichem Association of Privately Owned Pharmacies. 1959.

Intra Vascular Catheterization. Compiled and edited by Henry A. Zimmerman, M.D., B.S. (Pp. 782+xviii; illustrated. £6 6s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1959.

Peripheral Vascular Diseases. An Objective Approach. By Travis Winsor, M.D., F.A.C.P. With a foreword by Burrell O. Raulston, M.D. (Pp. 845+xviii; illustrated. £6 5s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1959.

Methods of Geographical Pathology. Report of the Study Group convened by the Council for International Organizations of Medical Sciences. Established under the joint auspices of UNESCO and WHO. Edited by Richard Doll. (Pp. 72. 9s. 6d.) Oxford: Blackwell Scientific Publications. 1959.

Trigeminal Neuralgia. Its History and Treatment. By Byron Stookey, A.M., M.D., and Joseph Ransohoff, M.D. (Pp. 366+xv; illustrated. 81s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1959.

Human Nutrition and Dietetics. By Sir Stanley Davidson, B.A.(Cantab.), M.D., F.R.C.P.Ed., F.R.C.P.(Lond.), M.D.(Oslo), A. P. Meiklejohn, M.A., B.Sc., D.M.(Oxon.), M.R.C.P.(Lond.), and R. Passmore, M.A., D.M.(Oxon.). With a foreword by Lord Boyd Orr, D.S.O., M.C., LL.D., F.R.S. (Pp. 844+xii; illustrated. 84s.) Edinburgh, London: E. and S. Livingstone Ltd. 1959.

Tuberculosis and Other Communicable Diseases. By J. Arthur Myers, M.D. (Pp. 499+xii; illustrated. £5 10s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1959.

Vocational Rehabilitation for the Physically Handicapped. By Louise M. Neuschutz. (Pp. 136; illustrated. 43s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1959.

Pancreatitis. A Clinical-Pathologic Correlation. By Herman T. Blumenthal, Ph.D., M.D., and J. G. Probstein, M.D. (Pp. 379+xiv; illustrated. 72s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1959.

Basic Physics in Radiology. By L. A. W. Kemp, B.Sc., Ph.D., F.Inst.P., and R. Oliver, M.Sc., F.Inst.P., A.M.I.E.E. (Pp. 329+xiii; illustrated. 35s.) Oxford: Blackwell Scientific Publications. 1959.

Hypnosis in Modern Medicine. Edited by Jerome M. Schneck, A.B., M.D. Second edition. (Pp. 389+xix. 66s.) Springfield, Illinois: Charles C. Thomas, Publisher. Oxford: Blackwell Scientific Publications. 1959.

BRITISH MEDICAL JOURNAL

LONDON

SATURDAY AUGUST 29 1959

ONCOGENIC PARTICLES

Reports on two newly discovered agents causing mouse tumours, and the application of precise quantitative techniques to the study of Rous sarcoma virus in tissue culture, have again stimulated the investigation of tumour viruses—or, for the more cautious, oncogenic particles.

The pioneer studies of L. Gross, recently reviewed,[1] showed that leukaemia could be induced in the C_3H strain of mice if they were inoculated in the first few hours of life with cell-free extracts of leukaemic or normal tissue from the AK strain, which has a high natural incidence of this disease. The agent was not present in the milk of AK mothers but was in the tissue of the embryos before birth, so Gross put forward the idea of "vertical transmission" from mothers to offspring *in utero* leading to a hereditary, but non-genetic, trait in the AK strain.

C. Friend[2 3] has now identified a different leukaemic agent which can be propagated even in adult mice by inoculation of leukaemic blood and spleen filtrates. This agent came originally from two mice with splenomegaly in a large batch inoculated with filtrates of Ehrlich ascites tumour, but its connexion with the Ehrlich tumour is doubtful. Several strains of adult mice are susceptible to it, and a characteristic of the disease is its relatively short incubation period. Enlarged, palpable spleens are found a week after inoculation and the white-cell count rises considerably in the second and third week owing to the appearance of abnormal mononucleated cells ("Friend cells"); this rise is accompanied by erythroblastosis and followed eventually by anaemia. There has been some doubt about the status of mouse leukaemias as malignant tumours and about their similarity to human leukaemias, so it is of interest that a panel of 16 pathologists who examined specimens decided independently that the condition was malignant; and, indeed, most diagnosed some form of leukaemia.[4] D. Metcalf and colleagues[4] have concluded that the Friend leukaemia is due to unrestricted proliferation of reticulum cells.

A confusing aspect of Gross's earlier work was the frequent appearance of malignant tumours of the salivary glands in C_3H mice inoculated with the AK leukaemic agent. These tumours now appear to be due to a second and rather remarkable agent isolated and studied by S. E. Stewart and B. E. Eddy and others. These workers and their colleagues reported in 1957[5] that extracts of leukaemic tissue from AK mice, if cultured in monkey kidney cells or mouse embryo cells *in vitro*, induced tumours, but not leukaemia, when inoculated into newborn mice or hamsters. The agent responsible has subsequently been propagated in tissue culture for many passages and has retained its oncogenic property. A striking feature of the agent is its ability to produce a wide variety of tumours after short incubation periods in various strains of mice or hamsters. Parotid and renal tumours including sarcomas and epitheliomas are most common in mice, but 23 different types of primary tumour have been identified.[6] Hamsters develop sarcomas of the kidney and various other organs as well as angiomas, but not epithelial tumours.[7] The agent has been named S.E. (Stewart–Eddy) polyoma virus.

Polyoma virus causes cell degeneration rather than proliferation in the tissue cultures of mouse cells,[8] and thus resembles another tumour virus, avian lymphoma, which has recently been found to grow in tissue culture with cell degeneration.[9 10] It will be of considerable interest if it can be shown that the same virus particles can cause either degenerative or neoplastic change, depending on the cell type or its physiological condition. Meanwhile cytopathic change in tissue culture provides a method for quantitative assay. So also does the discovery that the polyoma virus agglutinates red blood cells in a similar way to influenza virus.[11] Since antiserum to polyoma virus inhibits this haemagglutination, a simple test is now available to identify and titrate virus and antibody. This enabled W. P. Rowe and others to study the natural distribution of the virus in stocks of apparently healthy laboratory mice.[12] They found that in some stocks (in different research institutions) antibody to polyoma virus appeared in

[1] Gross, L., *Cancer Res.*, 1958, **18**, 371.
[2] Friend, C., *J. exp. Med.*, 1957, **105**, 307.
[3] —— *Ann. N.Y. Acad. Sci.*, 1957, **68**, 522.
[4] Metcalf, D., Furth, J., and Buffett, R. F., *Cancer Res.*, 1959, **19**, 52.
[5] Stewart, S. E., Eddy, B. E., Gochenour, A. M., Borgese, N. G., and Grubbs, G. E., *Virology*, 1957, **3**, 380.
[6] —— —— and Borgese, N. G., *J. nat. Cancer Inst.*, 1958, **20**, 1223.
[7] Eddy, B. E., Stewart, S. E., Young, R. D., and Mider, G. B., ibid., 1958, **20**, 747.
[8] —— —— and Berkeley, W., *Proc. Soc. exp. Biol. (N.Y.)*, 1958, **98**, 848.
[9] Sharpless, G. R., Defendi, V., and Cox, H. R., ibid., 1958, **97**, 755.
[10] Fontes, A. K., Burmester, B. R., Walter, W. G., and Iseler, P. E., ibid., 1958, **97**, 854.
[11] Eddy, B. E., Rowe, W. P., Hartley, J. W., Stewart, S. E., and Huebner, R. J., *Virology*, 1958, **6**, 290.
[12] Rowe, W. P., Hartley, J. W., Brodsky, I., Huebner, R. J., and Law, L. W., *Nature (Lond.)*, 1958, **182**, 1617.
[13] Halberstaedter, L., Doljanski, L., and Tenenbaum, E., *Brit. J. exp. Path.*, 1941, **22**, 179.
[14] Manaker, R. A., and Groupé, V., *Virology*, 1956, **2**, 838.
[15] Ruben, H., and Temin, H. M., *Fed. Proc.*, 1958, **17**, 994.
[16] —— —— *Virology*, 1959, **7**, 75.

practically all mice by 3 months of age, and that the virus could be isolated from mouth swabs, urine, and drinking-bottles. Polyoma virus thus appears to be a common commensal in laboratory mice even when spontaneous tumours are rare. Tumours can be produced artificially after inoculation only of newborn mice, however, so natural infection may occur later, at a time when the oncogenic activity of the virus cannot manifest itself, perhaps owing to maturation of immunity mechanisms. The incidence of natural infection was independent of the strain of mice, and, since there was great variation in different stocks of AK mice, this virus is thought to be unrelated to Gross's leukaemia agent, though its presence in the same mice could have led to the appearance of the parotid tumours observed by Gross in mice with induced leukaemia.

For experimental study of the nature of the neoplastic change it would be desirable to take normal cells growing *in vitro* and convert them at will under controlled conditions into malignant cells. This now seems possible for the first time with Rous sarcoma virus. The earlier reports of Halberstaedter and others[13] and of R. A. Manaker and V. Groupé[14] described morphological changes in cultured chick fibroblasts exposed to Rous sarcoma virus; now H. Ruben and H. M. Temin[15] have shown that a Rous virus particle interacts with a normal cell to produce a permanent inheritable change. The descendants of a single infected cell are altered morphologically and give rise to proliferative foci in culture. Unlike bacteria carrying bacteriophage, however, each cell releases a few virus particles per cell division. These workers[16] have also shown that the capacity of a cell to make Rous virus is very sensitive to *x* rays and differs greatly from the capacity for production of other viruses studied, which do not produce tumours. The radiation results have in fact suggested that synthesis of Rous virus is closely associated with the ability of a cell to divide.

A tumour may be considered as a clone of genetically altered cells—that is, a population originating from a single cell by mitosis. And, for some tumours of animals and birds at least, the new genetic pattern can be introduced at will by a virus which does not destroy the cell. Studies on phage-infected bacteria have shown that this type of genetic change can be subjected to fairly precise investigations. If the interaction between tumour viruses and cells can be subjected to a similar analysis, much information may be gained about the genetic behaviour of somatic cells and the control of cell differentiation. This in turn cannot fail to shed light on the problem of human malignant disease.

COXSACKIE INFECTION OF NEWBORN

Coxsackie B viruses, which are known to cause non-bacterial meningitis and Bornholm disease, have recently been detected as the cause of some more serious diseases. Just as the suckling mouse is highly susceptible but the adult mouse highly resistant to infection by these viruses, so the human infant is liable to develop severe or fatal disease from them, while adults rarely have more than a trivial illness. In the newborn, whether man or mouse, the viruses produce a systemic infection, damaging in particular the nervous and muscular tissues.

Since 1955 some reports of Coxsackie myocarditis of the newborn have appeared.[1–13] Sporadic cases were seen during seasonal outbreaks of Coxsackie B infection in the general community. The outbreaks among adults occur mainly in late summer or autumn, causing pleurodynia, non-bacterial meningitis, and "summer grippe." When a newborn baby was affected the mother often had history of minor febrile illness within a week of the infant's birth, and in two cases infection appeared to have been transmitted to the child *in utero*.[7 9] The high susceptibility of newborn infants helps rapid spread of infection in maternity units, and outbreaks with high mortality in such nurseries have been described in Southern Rhodesia[1] and South Africa.[2 3 10–13]

The clinical features of 25 reported cases were recently reviewed by S. Kibrick and K. Benirschke,[9] and eight additional cases were analysed by P. V. Suckling and L. Vogelpoel.[10] Illness generally began during the first fortnight of life, in the first week in 19 of the 33 cases. Common early signs were lethargy, difficulty in feeding, and fever; redness of the throat was a constant early sign in Suckling and Vogelpoel's series. Signs of heart failure, cardiac enlargement, abnormalities of rhythm, cyanosis, and pallor might draw attention to the severity of the illness. Progressive circulatory failure with enlarge-

[1] Montgomery, J., Gear, J. H. S., Prinsloo, F. R., Kahn, M., and Kirsch, Z. G., *South Afr. med. J.*, 1955, **29**, 608.
[2] Javett, S. N., *et al.*, *J. Pediat.*, 1956, **48**, 1.
[3] Gear, J. H. S., Measroch, V., and Prinsloo, F. R., *South Afr. med. J.*, 1956, **30**, 806.
[4] Dekking, F., *Ned. T. Geneesk.*, 1955, **99**, 2676.
[5] Van Creveld, S., and De Jager, H., *Ann. Paediat.* (*Basel*), 1956, **187**, 100.
[6] Verlinde, J. D., Van Tongeren, H. A. E., and Kret, A., ibid., 1956, **187**, 113.
[7] Kibrick, S., and Benirschke, K., *New Engl. J. Med.*, 1956, **255**, 883.
[8] Sabin, A., *Year Book of Pediatrics*, 1957–58 Series, p. 269. Chicago.
[9] Kibrick, S., and Benirschke, K., *Pediatrics*, 1958, **22**, 857.
[10] Suckling, P. V., and Vogelpoel, L., *Med. Proc.*, 1958, **4**, 372.
[11] Simenhoff, M. L., and Uys, C. J., ibid., 1958, **4**, 389.
[12] Naudé, W. Du T., Selzer, G., and Kipps, A., ibid., 1958, **4**, 397.
[13] Kipps, A., Naudé, W. Du T., Don, P., and Cooper, E. D., ibid., 1958, **4**, 401.
[14] Hosier, D. M., and Newton, W. A., *A.M.A. J. Dis. Child.*, 1958, **96**, 251.
[15] Movitt, E. R., Lennette, E. H., Mangum, J. F., Berk, M., and Bowman, M. S., *New Engl. J. Med.*, 1958, **258**, 1082.
[16] McLean, D. M., Croft, C. C., Prince, J. T., and Heckmann, E. E., *Ohio med. J.*, 1957, **53**, 907.
[17] —— Walker, S. J., and Bain, H. W., *Canad. med. Ass. J.*, 1958, **79**, 789.
[18] Weinstein, S. B., *New Engl. Med. J.*, 1957, **257**, 265.
[19] Kagan, H., and Bernkopf, H., *Ann. Paediat.* (*Basel*), 1957, **189**, 44.
[20] Bing, H. I., *Acta med. scand.*, 1933, **80**, 29.
[21] Heckscher, H., ibid., 1933, **80**, 251.
[22] Fletcher, E., and Brennan, C. F., *Lancet*, 1957, **1**, 913.
[23] —— —— ibid., 1958, **2**, 585.

ment of liver bore a grave prognosis. Serial electrocardiograms generally showed changes in the S-T segment and T wave. The disease sometimes followed a biphasic or relapsing course. Several infants died shortly after sudden collapse early or late in the illness. Of 33 babies, 23 died, 17 during the first week of illness and seven of these within 24 hours of its onset. No sequelae were noted in children who survived, and the possibility that recovery can be complete was also suggested by the rapid repair of patchy myocardial necrosis found by M. L. Simenhoff and C. J. Uys[11] at necropsy on four babies who died after periods of illness ranging from 2 to 11 days.

Though there is no known specific treatment for Coxsackie virus infection, Suckling and Vogelpoel recommended vigorous measures to combat heart failure in the infants. Of their four fatal cases, two died almost untreated in the early acute phase of illness, whereas two who received active treatment from the early stage survived until the repair stage of the disease.[10] Cortisone, which increases the severity of this and similar infections in experimental animals, may be contraindicated; but recovery has been recorded after treatment with it in Coxsackie myocarditis.[2 14] Prevention may be difficult, but the gravity of this infection of infants is yet another reminder of their vulnerability, of the importance of minimizing their contact with older persons suffering even from very minor symptoms, and of the special dangers of concentrating susceptible newborn infants in nurseries.

Coxsackie viruses are classified in two groups, A and B, differentiated by the pattern of experimental disease in suckling mice; within each group serologically distinct types are designated numerically. Except for a single report of type A1 infection of an adult with pericarditis,[15] Coxsackie viruses associated with cardiac disease have belonged to group B. Types B3 and B4 have been associated with neonatal myocarditis, except for isolation of type B2 virus from the heart of one case.[3] Type B2 virus was also isolated from the stools of an older child with myocarditis.[16] Type B5 Coxsackie virus was isolated from the stools of four children with benign pericarditis,[17] and falling titres of antibody to this virus were found in sera taken from an adult late after the onset of pericarditis.[18]

Though Coxsackie myocarditis of the newborn has not been reported from Great Britain, cases may have occurred. Infants with symptoms suggestive of it should be investigated, and the virus might be isolated from stool specimens. At necropsy the pathologist should remove with sterile technique a piece of heart muscle, and perhaps other tissues, for attempted virus isolation. It is worth bearing in mind that in the newborn baby the infection may be generalized, with particular damage to the central nervous system and liver,[7 9] while Coxsackie myocarditis and pericarditis affecting older children have been reported by several workers.[14 18 19] The association of pericarditis with Bornholm disease of adults was reported in 1933,[20 21] and laboratory evidence of Coxsackie virus infection in acute benign pericarditis has recently been described.[15 19 22 23] Cocksackie viruses are common among the enteric virus infections of man, and it is interesting to speculate whether systemic spread of these agents may cause inapparent as well as overt cardiac damage, and whether this may be related to myocardial disease in later life.

SUPPORT FOR CANCER RESEARCH

For 36 years the British Empire Cancer Campaign has been subsidizing research into cancer in many different centres. Its function is slightly different from that of the Imperial Cancer Research Fund, which was founded 25 years earlier but which has always confined itself to supporting whole-time cancer research workers in its own research laboratories. The policy of the British Empire Cancer Campaign, on the other hand, has been to give grants to cancer research workers in hospitals and institutions over which it has no direct control. The existence of two separate cancer research organizations has sometimes given rise to confusion in the mind of the public, but this is likely to be lessened when the Imperial Cancer Research Fund has completed the new research laboratories which it is building in Lincoln's Inn Fields close to the Royal College of Surgeons.

During the year 1958 the total expenditure on research financed by the central organization of the British Empire Cancer Campaign amounted to more than £600,000, and the recently published Annual Scientific Report[1] gives an account of the many different research activities supported by the Campaign. The reader who glances quickly through the 600 pages of the report must be impressed by the great variety of the work in progress in so many different branches of biology, biochemistry, physics, and pathology, and we can here mention only one or two of the projects which seem to be of special interest at the present time.

A remarkable experiment has been in progress over a seven-year period at the Animal Supply and Research Unit, Edinburgh. The experiment began in

[1] Thirty-sixth Annual Report of the British Empire Cancer Campaign—Part II. The Scientific Report. Obtainable from the B.E.C.C., 11, Grosvenor Crescent, London, S.W.1.

March, 1952, when 19 hens were maintained in a standardized environment at a temperature of 65° F. (18° C.), a relative humidity of 60%, and with artificial light only. All these 19 birds eventually succumbed to malignant tumours of the ovary or oviduct. Over the same period from a pen of 17 closely related hens kept under a normal system of housing only three birds died, none with tumours. It is suggested that absence of environmental fluctuations may have led to long periods of sexual activity, and that this may be the primary cause of this type of cancer. This important observation is of special significance in relation to endocrine carcinogenesis.

While some of the studies on experimental radiation are directly concerned with the potential hazards associated with prolonged exposure to ionizing radiation and others with the use of radiation as a therapeutic agent, the majority constitute an attack on the basic problem of discovering more precisely the way in which living cells respond to radiation, the factors which modify this response and the underlying causes in terms of physical and chemical changes which take place in the cell at the time of irradiation.

In the field of clinical and comparative pathology many different research projects are described in the report, and some of them have a direct bearing on the diagnosis and treatment of human cancer. There is evidence here of the growing interest in cytological methods for the diagnosis of malignant disease and their efficacy in the early recognition of cancer of the uterine cervix. Similar methods are now being successfully employed in the diagnosis of cancer of the stomach. At more than one centre work is being done confirming the efficacy of recently described techniques for isolation of tumour cells from the blood. Among the interesting applications of these techniques is a demonstration of the extent to which the liver removes tumour cells from the blood; this can be assessed by comparing the frequency with which the cells can be identified in blood samples from the portal and hepatic veins.

This report once again shows what a great service the British Empire Cancer Campaign has rendered to the research departments of universities and medical schools, and especially to hospitals in the National Health Service. The long-continued support of research at such hospitals as the Middlesex and St. Mark's, to mention only two which have been helped by the Campaign each year from its foundation in 1923, has made possible the completion of long-term research projects which clearly are now beginning to bear fruit.

CET ANIMAL EST MÉCHANT . . .

Imitating some of the pharmaceutical houses, the American Medical Association has recently issued "a newspaper of American Medicine" called the *A.M.A. News*. Appearing fortnightly, it highlights the A.M.A.'s medico-political programme. A glance at one or two numbers shows the A.M.A.'s fear of Britain's N.H.S. For example, it published in the issue of June 29 a few paragraphs under the heading "British Doctors Ready to Strike." In the issue of July 27 the story reappeared under "British Doctors Threaten Strike," and on another page is reprinted, without comment, a piece from "Chattanooga, Tenn. News-Free Press," with its "British socialized medical plan, which costs many billions in taxes annually *while denying individuals even the choice of their own doctor.*" (Our italics.) Patients have free choice of doctor in Great Britain's National Health Service, possibly even freer choice than patients in the U.S.A., whose freedom to choose is restricted by their ability to meet the doctor's bill. The *A.M.A. News* does a disservice to its readers in allowing the facts to be misrepresented.

Another example of inaccuracy from this newspaper (July 27): "Since its inception in 1945, M.D.s in Great Britain have been given two small pay increases." N.H.S. came into operation in 1948, not 1945. Since then there have been three increases in pay, one of which, the Danckwerts award of 1952, certainly cannot be described as small.

A.M.A. News of July 27 also gives some extracts from the testimony to Congress of Dr. R. B. Robins, member of A.M.A. Board of Trustees, whom many of us met on his recent brief visit to England. Dr. Robins is quoted as saying: "I saw medicine put on an assembly-line basis: I saw numbers supplanting names. I saw a process so coldly impersonal that I was reminded of a machine stamping out file cards." Dr. Robins must have been reading *A.M.A. News*!

Of course Britain's N.H.S. is imperfect, and has been criticized often enough in this *Journal*. The B.M.A. has set up the Porritt Committee to look into the imperfections and to seek remedies. But if our colleagues in the A.M.A. want to be well prepared to deal with governmental plans for introducing compulsory health insurance into the U.S.A. they would be wiser, we suggest, to find out how far American Medicine falls behind in its services to the great American public.

Here, for example, is what Dr. Paul R. Hawley, director of the American College of Surgeons, says about American surgery[1]: "It is now reliably estimated that to-day one half of the surgical operations in the United States are performed by doctors who are untrained or inadequately trained to undertake surgery." At least we can say, without false modesty, that this does not happen under the much-maligned N.H.S. Perhaps a report by British doctors on the disadvantages of the American medical system is long overdue.

[1] *M.D. Medical News Magazine*, July, 1959, p. 68.

LEUCOCYTE AGGLUTININS

Iso-agglutinins against leucocytes are now known to be found sometimes in the sera of patients who have received repeated transfusions, and they can be a cause of febrile transfusion reactions.[1] More recently, the development of iso-agglutinins as the result of differences between the leucocyte antigens of a mother and her foetus has been described. R. Payne and M. R. Rolfs[2] tested the sera of 144 pregnant multiparous women, all of whom had had four or more pregnancies, the sera of 20 women who had never been pregnant or transfused, and the sera of eight patients who for various reasons were expected to have developed leucocyte agglutinins. Each serum was tested separately against a panel of leucocyte suspensions derived from 10 different group-O subjects. A positive result was scored if the heat-inactivated sera agglutinated two or more of the test leucocyte suspensions on two different occasions.

The results of this laborious work are interesting. Twenty-five (17%) of the women in Group I had sera containing leucocyte agglutinins, usually at low titres (8 or less), compared with none of the women in the control series. The foetus appeared to be the only stimulus in 18 of the women since they had not been transfused. None of the sera agglutinated the patients' own leucocytes. Some of the patients included in Group II had sera containing immune anti-A or Rh antibodies, but the data were too few to determine whether patients producing anti-red-cell antibodies produced anti-leucocyte antibodies unusually readily. It seemed clear that the formation of the leucocyte antibodies was not related to the maternal ABO and Rh group.

The next stage in Payne and Rolfs's investigation was to test the leucocytes of the infants after birth and of the fathers against the maternal sera. On the hypothesis that the antigens giving rise to the agglutinins were derived from the foetus, the infants' leucocytes and those of the father should be invariably agglutinated. The results of such tests appear to prove the hypothesis. The leucocytes of 10 out of 12 infants were agglutinated, and in one case in which the present infant's leucocytes were not agglutinated it was found that the leucocytes of three other siblings in the family were agglutinated. (This is perhaps analogous to the birth of an unaffected Rh-negative infant by a mother who has already had several infants affected with haemolytic disease of the newborn, the father being Rh-positive but heterozygous.)

The leucocytes of 12 out of 13 fathers were agglutinated by the maternal sera as expected; the remaining father may not in fact have been the father of the child in question. More extensive family studies were carried out in several instances, and in one family a leucocyte factor agglutinable by the maternal serum could be traced through three generations.

These noteworthy studies are of practical as well as theoretical importance. They may provide an explanation for hitherto unexplained febrile transfusion reactions occurring in multiparous women. The anti-body-containing sera, too, may prove to be more useful in the determination of leucocyte iso-antigens than sera from patients who have received many transfusions, which seem likely inevitably to contain a mixture of antibodies. However, as opposed to antibodies developed by a mother against foetal red-cell antigens, leucocyte iso-antibodies in the maternal serum do not seem to harm the foetus or newborn infant. Transient leucopenia may occur, but Payne and Rolfs report that this is infrequent.

[1] *Brit. med. J.*, 1958, **1**, 1467.
[2] Payne, R., and Rolfs, M. R., *J. clin. Invest.*, 1958, **37**, 1756.

DISPOSAL OF RADIOACTIVE WASTE

Until 1954 there was no special legislation governing the disposal of radioactive waste; it was subject only to the provisions of the Public Health Acts. The controls established in that year over the radioactive wastes produced by the United Kingdom Atomic Energy Authority[1] have formed the pattern for the proposed similar controls over the waste produced during the operation of nuclear reactors to be operated by the Central Electricity Generating Board[2]: they make illegal any discharge of radioactive waste from premises of the U.K. Atomic Energy Authority unless authorized by the Ministries of Housing and Local Government and of Agriculture, Fisheries and Food after consultation with the appropriate local authorities and similar public bodies. Thus the two principal producers (now or in the future) of radioactive wastes have to comply with legislation which is probably more stringent than any other form of legal control over the disposal of toxic wastes. The emission of reactor coolant gas at Harwell and Windscale, the discharge of radioactive effluent to the Thames from Harwell, Aldermaston, and Amersham, and to the sea at Windscale and Dounreay, the dumping of solid radioactive waste at sea—all are controlled by the terms of authorizations from Government departments.

While these radioactive wastes and the much discussed fission products separated in the chemical processing of nuclear fuels (which will not be done at the power stations but at Windscale and possibly other selected sites) are handled by staff trained and well versed in the hazards and are, moreover, under adequate legislative control, more concern may be felt over the other premises (about one thousand in number) where radioactive materials are used. More than 90% of the radioactivity used in industry and hospitals comes from solid closed sources, which normally produce no waste. Ultimately, the source will have decayed to too low a level for its purpose (for instance, the detection of flaws in welds). If the isotope used has been made by irradiation in a reactor (as cobalt-60 and iridium-192), the source can be reactivated and re-used without waste. However, if the isotope is a chemically separated fission product (as strontium-90 and caesium-137) reactivation is not possible, and the source will constitute a highly active waste. It has been announced

[1] Atomic Energy Authority Act, 1954.
[2] Nuclear Installations (Licensing and Insurance) Act, 1959.
[3] *House of Commons Official Report*, April 7, 1959, Col. 5.
[4] Kenny, A. W., *Bull. Wld Hlth Org.*, 1956, **14**, 1007.
[5] Key, A., and Kenny, A. W., *Proc. Inst. civ. Eng.*, 1952, 280.

that, by informal temporary arrangement, this and other waste too active for disposal by conventional methods can be taken by the Atomic Energy Research Establishment at the user's expense.[3]

The use of isotopes as open sources in research laboratories and hospitals does not normally produce very active waste. Disposal by conventional methods, sometimes after storage to allow decay, is usually possible. It has been advocated that specific limits for disposal in these ways should be laid down, but the materials concerned have a wide range of toxicity, and consequently general limits, if they are to insure that the most toxic materials do not approach hazardous level, will be much too restrictive for the least toxic. However, it may be taken as a rough rule that an average concentration of 2½ millicuries of isotopes emitting beta or gamma radiation per 1,000 gallons of sewage flow from an institution is acceptable.[4] For solid waste, the occasional disposal in the dustbin of microcurie amounts would be no more dangerous than the similar disposal of luminous clock dials.

At present there is a central record of users of radioactive materials[5] and a central system for disposal of radioactive waste[3]—an arrangement which, though informal, enables effective control to be exercised. It is to be expected that the promised legislation will give legal backing to the present arrangements and provide additional powers which may be needed in the future.

LIVING IN CARAVANS

The Ministry of Housing and Local Government has arranged for a one-man inquiry into the use of caravans as homes in England and, perhaps more particularly, in Wales. The investigator, Sir Arton Wilson, will examine the adequacy of the present law, but the making of recommendations does not come into his terms of reference. Local authorities will wonder how much help this inquiry is going to give them, for in some districts where there has been an influx of caravanners speculators have dumped caravans on to very unsatisfactory unlicensed sites, which can be closed down only after expensive litigation. A site may be used for camping purposes for 42 consecutive days or for 60 days in any 12 consecutive months without a licence from the local authority. In its memorandum of evidence[1] to the Ministry's investigator the Society of Medical Officers of Health states that a reduction in the number of days allowed before a licence has to be applied for would assist local authorities in controlling undesirable sites.

The present law relating to residential caravans (holiday caravans are not under consideration here) is by no means exhaustive. Under the Town and Country Planning Act, 1947, a site licence can be refused only on the ground of "damage to amenities." This vague concept is one on which a local authority may easily be defeated should the applicant appeal to the courts. The public health legislation is still contained in Sections 268 and 269 of the Public Health Act, 1936. Section 268 concerns itself with the abolition of nuisances in "tents, vans, sheds and similar structures." It has come down unchanged from the Housing of the Working Classes Act, 1885, being designed to apply to nomads and tinkers. It is arguable how far its provisions apply to-day. Section 269 defines movable dwellings as including "any conveyance whether on wheels or not" and may thus fairly be taken to include the contemporary trailer caravan. The section empowers local authorities to lay down conditions for the granting of licences for single caravans and to persons seeking to establish caravan sites. These conditions are, however, few. In the case of a single caravan the local authority may demand no more than "a supply of wholesome water sufficient for domestic purposes," together with arrangements for "securing satisfactory sanitary conditions." Such ill-defined phrasing can lead to much legal argument. This section also permits local authorities to impose a condition requiring the removal of a caravan at the end of a specified period.

When a site licence is granted the local authority may in addition stipulate the number of vans to the acre. Many sites are admirably managed; others are no credit to their owners. There would seem to be no right in law to demand adequate roads and paths, hard-standings, lighting, or fire precautions, and the Society of Medical Officers of Health suggests that minimum statutory standards should be laid down. Nowhere is the number of human beings (or domestic animals) which may be crammed into a single caravan laid down, nor are any minimum dimensions defined—although a maximum size of 22 × 7.5 ft. (6.6 × 2.25 m.) is fixed by the Ministry of Transport to prevent obstruction on the highway. There is no restriction on the rent chargeable, no limit to the amount of place money (sums of up to £80 per caravan are known to have been charged with perfect legality); and the site operator, unlike any other landlord, may evict without any obligation to provide alternative accommodation. Caravanners thus often tend to refrain from criticism of the unscrupulous type of site operator who trades on the misfortunes of the homeless. It has been estimated that between one-third and one-half of the present 300,000 permanent caravanners in the country live in caravans from choice. Many of them are in occupations demanding mobility.

The dangers to the health of families living permanently in caravans tend in the main to be those associated with substandard housing; shortage of space causes overcrowding, with all that that implies. The memorandum of evidence of the Society of Medical Officers of Health mentions in particular the adverse effects of being unable to dry clothes properly. Nearly everyone agrees that caravans are unsuitable as permanent homes for families with young children. The suggestion that the "good" caravan is better than the bad house may be in part true, but it is an argument not so much for the retention of the caravan as for the demolition of the bad house and its speedy replacement by a good one.

[1] *Publ. Hlth (Lond.)*, 1959, **73**, 314.

British Medical Association

JOINT ANNUAL MEETING WITH THE CANADIAN MEDICAL ASSOCIATION, EDINBURGH, 1959

SUMMARY OF PROCEEDINGS

FIRST PLENARY SESSION—TRENDS IN MODERN MEDICINE

Wednesday, July 22

Dr. NORMAN H. GOSSE (Halifax, Nova Scotia) took the chair at the opening Plenary Session, at which a number of Canadian doctors spoke on "Trends in Modern Medicine."

Virus Infections

Professor A. J. RHODES (Toronto) said that the number of human viruses known to virologists had increased from 36 in 1939 to more than 150 at the present time. Of these 150 only five defied isolation in the laboratory. Viruses could be classified into five groups: Basophilic viruses with five members, related to the psittacosis virus and causing virus pneumonia, sensitive to certain antibiotics; nine influenza viruses in addition to influenza A; 29 anthropod-borne viruses causing encephalitis in the Americas and Australia, haemorrhagic disease in Russia, and Kyasanur Forest disease in India; enteroviruses; adenoviruses.

Virus infections were the commonest infections in general practice, and, in contrast to bacterial infections, were resistance to antibiotics.

Techniques of isolation had been simplified, often permitting the identification of viruses as early as 24 hours after inoculation of material from the patient. Isolation of a virus from a patient did not necessarily mean that the patient was suffering its effects, since carrier states were common. The clinical manifestations of infection with any one virus could be protean in the same epidemic.

Discussing vaccination with live and dead poliomyelitis virus (one of the enteroviruses), Professor Rhodes said that he did not think the virulence of live attenuated virus would be enhanced by human passage. The adenoviruses, of which there were 20 types, might be more important than enteroviruses. They caused acute respiratory disease in military recruits; virus pneumonia; laryngo-conjunctival fever; common colds; epidemic keratoconjunctivitis; and sporadic non-bacterial conjunctivitis.

Pathogenesis of Anaemia

Professor K. J. R. WIGHTMAN (Toronto) speaking on recent concepts in the pathogenesis of anaemia, discussed the ways of reducing the red-cell mass. In aplastic anaemia there was an absence of red-cell precursors in the bone marrow, which in certain cases might be due to some auto-immune factors; in the anaemia associated with some tumours of the thymus the marrow was depleted of red-cell precursors, but on removal of the tumour these cells reappeared. Failure of red-cell production occurred in the absence of dietary factors.

The only stimulus to erythropoiesis was anoxia, and a hormone, erythropoietin, was thought to be concerned in this. Its site of production was unknown and it had never been isolated or characterized. Deficiency of erythropoietin was thought to cause the anaemia of chronic renal disease. Some conditions, such as congenital spherocytosis, were caused by an enzyme dyscrasia, and alterations in enzyme content of the red cell, either constitutional or acquired, were responsible for the appearance of some abnormal haemoglobins.

Professor Wightman concluded his informative paper by describing alterations in plasma volume met with in various diseases of the blood.

Nuclear Energy Establishments

Dr. C. GORDON STEWART (Deep River, Ontario) gave an account of the physics of nuclear fission and its application to the design and structure of atomic plants for the production of radioactive materials. Describing how the staff of such plants were protected against the dangers of radiation, he gave a dramatic demonstration of an instrument for giving warning of high levels of radiation, which was carried by personnel open to special risk. These and other measures taken in the plant of which he was in medical charge had resulted in a complete absence of serious cases of radiation illness despite two incidents in which there had been an accidental release of gamma radiation.

Treatment of Psychiatric Illness

Professor R. O. JONES (Halifax, Nova Scotia) gave an account of changes during the last 17 years in the public's attitude to psychiatric illness. Much more money was now being spent on psychiatric services. This had been accompanied by a lessening of the social disgrace felt at having to seek psychiatric advice, and an increased readiness by the public to do so. A feature of the period under review was a decrease in the number of patients admitted to the mental hospital, and a rise in those admitted to the general hospital for psychiatric treatment and in those treated at home. This he attributed to the more widespread use of electropexy since 1948, and more recently of tranquillizing and psychostimulating drugs.

He felt that the greatest change he had seen was the introduction of electropexy for affective disorders, especially endogenous depression, the prognosis of which was now completely altered. No less than 85% of admissions of voluntary patients for psychiatric disturbance were now to a general hospital.

SECOND PLENARY SESSION—PROBLEMS OF AN AGEING POPULATION

Friday, July 24

Biological Aspects of Ageing

Sir ARTHUR THOMSON (Birmingham) took the chair, and Professor P. L. KROHN (Birmingham) opened with a paper on biological aspects of ageing. None of the theories purporting to account for the gradual loss of vitality and increasing likelihood of death as we became older was generally acceptable. Proficiency in particular tests rose to peaks at different ages; thereafter there were different rates of decline, which suggested that the individual systems of the body aged at very different rates. The life span of rodents could be increased by restricting calorie intake so that the control of nutrition, and in particular the control of obesity, might play an important part in increasing life span. The diet giving the maximum rate of growth was not associated with long life. The long post-reproductive period of life in the human female greatly restricted the opportunity for an increase in average life span to occur by the operation of an evolutionary factor. It also meant that the effects of those genes whose deleterious effects did not find expression till late in life could only be postponed and not eliminated.

Was ageing a local or systemic phenomenon? Professor Krohn was interested in research work on the ovary, in which decline in the number of oocytes gave a quantitative expression of ageing. Could an ovary be rejuvenated by transfer to a younger environment.

Demographic and Social Aspects

Dr. J. H. SHELDON (Wolverhampton) said that although ageing presented society with problems, it was less than fair

to regard age as a problem, for the old made notable contribution to our social integrity. Up to the early seventies at least they were donors rather than debtors. It was the proportion of old people which mattered to society. Though within the next 20 years there would be an increase in the number of old people in Britain, the problems might not be as severe as were feared, owing to the improvement in birth rates since the war. While it took 65 years to grow an old man, it took only 20 years to make someone old enough to look after him.

The declared policy in Britain was to help elderly people to live in their own homes as long as possible. Till the age of 75 the vast majority could look after themselves; after 75 the capacity to lead independent life became precarious. As Dr. Sheldon saw it, the major problem was to promote and continue those features in the structure of our society which would allow human ties to continue for the comfort and care of the elderly.

The Mental Health Problem

The mental health problem of ageing was discussed by Professor M. ROTH (Newcastle upon Tyne). The expectation of mental illness, as reflected by first admission rates to mental hospital, increased with advancing age, and suicide rates also reached a peak in old age. Evidence suggested that in the "functional" psychoses of old age genetic loading was smaller and exogenous factors were relatively more important than in comparable illnesses in earlier life.

One of the major advances in medicine during the past few decades had been the recognition that much which formerly passed as the effect of intrinsic ageing was due to disease which was susceptible to mitigation or cure. Medical advance might offset any tendency to an increase in invalidism due to the ageing of a population, as had been recently demonstrated by an investigation in Sweden.

Preventive Aspects of Illness in the Elderly

Dr. W. F. ANDERSON (Glasgow) began his paper on preventive aspects of illness in the elderly by stressing that hospital admission should be available promptly for elderly ill people on the request of the general practitioner. Their treatment in hospital should be brief, and they should be returned home as soon as possible. Rutherglen general practitioners could refer people over 55 years of age to a consultative health centre for older people started by the medical officer of health in co-operation with the regional hospital board.

The functions of the centre were: to promote health and prevent disease and thus maintain elderly people in a sound state of physical, mental, and social well-being; to complete a register of old people living within the district; to search for early and unsuspected disease; to integrate treatment with social circumstances through the facilities of the local authority; to give advice on services available; and to carry out research into the ageing process. Examination of 1,200 people had shown, among other findings, the great importance of obesity as a source of disability. The centre was a joint effort to prevent illness and to keep older people active and healthy in their own homes.

Geriatric Services

Dr. T. N. RUDD (Southampton) thought that the principal obstacle to happiness in old age was the unfavourable psychological climate. The reasons for this prejudice included the supposed burden of old age on the producing community, physical and mental frailties of the old, and the development of an attitude among younger people of rejecting their elders. This attitude was as widespread in doctors and nurses as in others. Adequate care required a geriatric team in which the medical social worker was as important as the physician.

The influence of morale in old age could not be overemphasized. Every effort to preserve the personality and to arouse interest must be made. Dr. RUDD thought that the prevention of relapse of the recovered case after his discharge from hospital was one of the most serious unsolved problems. He suggested that the geriatric outpatient clinic and day hospital might find their most useful role in this.

GENERAL SESSION

Thursday, July 23

Experimental Diabetes

Under the chairmanship of Dr. WILDER PENFIELD (Montreal), Professor CHARLES H. BEST (Toronto) reviewed the development of research into experimental diabetes from 1919 to 1949. Until 1921 there were many differences of opinion over the part played by the pancreas in diabetes, the two standard British (Starling) and Canadian (Macleod) textbooks of physiology holding quite opposite views. Professor Best briefly reviewed the work of all the great research workers in this field from Banting onwards. Speaking about the development of the various types of insulin, he referred to the contribution of his own colleagues in Toronto and of Hagedorn in introducing the zinc and protamine compounds and of the Danes in producing the "lente" insulins. He felt that we were, at present, merely on the threshold of progress, that purer forms of insulin would continue to be developed, and that an oral form of insulin would become a standard treatment within the next decade. Much active research was in progress on the mode of action of insulin. The new oral sulphonamide products, such as tolbutamide, had a very limited place in the treatment of diabetes. They were only active where functional β cells were present, and they seemed to exert their action through the liver as well as the pancreas.

Edinburgh's Contribution to Medical Education in Canada

Professor LLOYD G. STEVENSON (Montreal) read a delightfully anecdotal paper on the contributions of Edinburgh University to medical education in Canada, pointing out that in the 18th century the medical education given at Edinburgh was the most practical, the cheapest, and the quickest in the world. It was for this reason, he believed, that Edinburgh attracted so many Colonial students. In 1810 the first Canadian qualified at Edinburgh, he was followed by an average of 7 to 12 graduates each year. There was now a two-way traffic between the Scots and the Canadians, and in the last few years graduates from Edinburgh had taken over professorial chairs in Canadian universities and Canadians had been appointed to the teaching staffs of the Edinburgh medical school.

Present Status of Collagen Disease

LORD COHEN OF BIRKENHEAD (Liverpool) gave a masterly account of the present status of collagen disease, first tracing the historical origins of this pathological conception. There were now nearly 20 recognized collagen diseases, conditions presenting differing characteristic clinical patterns, but some patients described by Lord Cohen had clinical features of more than one type of a collagen disease. Generalizations might be dangerous, but there were in this group of conditions certain basic pathological changes that might with time be more closely related to specific aetiological causes.

Recent advances had well illustrated a new and dynamic approach to collagen diseases. Polyarteritis nodosa and other collagen disorders had been shown to present many features of allergic antigen–antibody reactions with hyperglobulinaemia, eosinophilia, and false-positive serological tests for syphilis. Corticosteroids had been shown to control many of the effects of collagen diseases. A history of sensitization to antibiotics, sulphonamides, gold, vaccines, and sera had often been noted. The latest advances were related to the theories of autosensitization.

which had so far been shown to be responsible for many cases of Hashimoto's disease, myxoedema, and lupoid hepatitis. It was very possible that here lay the explanation of the causes of collagen disorders. Lord Cohen concluded by pointing out the dangers of a too ready acceptance of "collagen diseases" as a convenient label for the diagnostically destitute: the use of facile labels for clinical conditions was wrong and degrading.

Treatment of Breast Cancer

Professor JOHN BRUCE (Edinburgh) presented his views on the management of breast cancer and said he would try to clear up some confused thoughts on the attitudes of "the Edinburgh School." There were still over 9,000 deaths a year in women from breast cancer in Great Britain. In 1940 a group at Edinburgh decided to review the position with a view to improvements. At that time radical mastectomy, including clearance of the axilla, had been since the days of Halsted the accepted treatment for almost all cancers of the breast.

Radiotherapy was then a developing tool, and the Edinburgh group thought it necessary to try out a combination of removal of the tumour together with intensive radiotherapy to the axilla and chest. It was an accepted fact at that time, as it was at the present time, that cases where the growth was confined to the breast did well, while those in which spread had occurred did uniformly badly. Records of this method of treatment—local mastectomy and radiotherapy—had been carefully kept for over 15 years, and comparisons with other methods had been attempted. Though this was difficult, it was possible to make valid comparisons by including all cases over a period of five or more years. If this was done, there were in the majority of comparable series few significant differences between the results of the Edinburgh technique and those of standard radical mastectomy.

The Edinburgh experiment was now really at an end. There were now a number of different techniques available to treat cancer of the breast, and appropriate therapy should be arranged to meet the individual problems of each case.

New Appliances

A SIMPLE METHOD FOR COLLECTION OF FAECAL AND URINE SPECIMENS

Mr. C. SANDERS, F.I.M.L.T., F.R.M.S., Medical Division, Atomic Energy Research Establishment, Harwell, writes: The collection of specimens of faeces from patients has always been an unpleasant one for the nursing staff and an embarrassing one for the patient, especially when the whole faecal sample is required for examination, since this involves the transfer of the specimen to a suitable container for dispatch to the laboratory.

Biological monitoring of persons who have been accidentally exposed to certain radioactive substances may require the examination of all specimens of faeces covering a period of days or even weeks. For example, the body excretion of caesium and strontium is measured by analysis of the total faecal specimen. These persons would normally be carrying on work in the usual way and would therefore have to collect the faecal sample themselves, both during working hours and at home when off duty. It is with this possibility in view that the following simple piece of equipment has been designed to provide a suitable and non-embarrassing method for the collection of faeces.

The apparatus consists of a support frame (Fig. 1) which is made from 18-gauge aluminium or dural. The frame fits inside the conventional lavatory pan basin, the support flanges of the frame resting upon the porcelain rim so that the lavatory seat can then be lowered into its normal position. The containers for the faeces consist of a waxed "mono container" of 7 in. (17.8 cm.) diameter which is placed on the platform of the frame and is retained in position by means of three small locating lugs. Waxed lids of the press-in type are provided with each container, and for ease in removal the lid is fitted with a small tag consisting of 1-in. (2.5-cm.) adhesive plaster which is folded over the edge of the lid and fixed in position by means of an ordinary wire staple.

To facilitate the removal of the sample, the waxed container is lined with thin P.V.C. sheeting simply by placing an 18-in. (45-cm.) square of the material over the

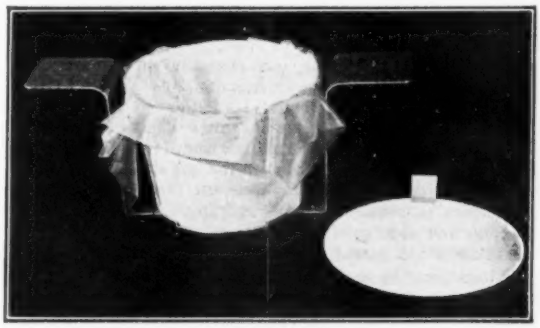


FIG. 1.—Photograph of apparatus.

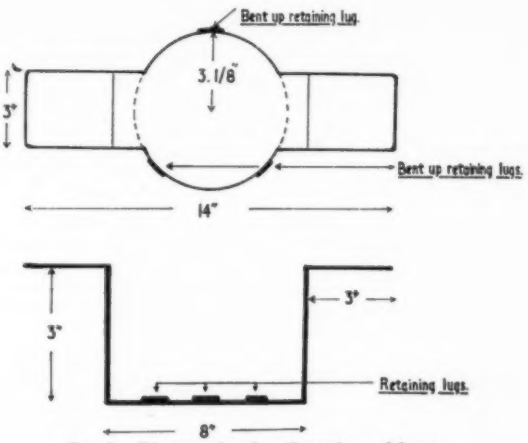


FIG. 2.—Diagram showing dimensions of frame.

carton and pressing this into position by means of another container. The use of the P.V.C. liner makes it a simple matter to remove the sample for analysis when delivered to the laboratory; furthermore, the P.V.C. may be ashed with the specimen, since this material does not interfere with the estimation of caesium or strontium.

By replacing the waxed container with a wide-mouthed enamel or stainless-steel jug of suitable height, and moving the frame to the front portion of the lavatory pan, the apparatus can be used for the collection of female urine samples. The frame is easily cleaned or sterilized, as there are no crevices to harbour contaminating material. The dimensions of the frame are given in Fig. 2. The waxed containers are obtainable from Mono Containers Ltd., Cumberland Avenue, Park Royal, London, N.W.10, and cost, complete with lids, £7 5s. 6d. per 100. Since the containers fit inside each other, storage space is reduced to a minimum and a reasonably large number can be kept ready for immediate use in the event of an emergency.

To-day's Drugs

With the help of expert contributors we publish below notes on a selection of drugs in current use.

Pacatal (William R. Warner).—This is pecazine (mepazine in the U.S.A.), a member of the large group of drugs derived from phenothiazine. Its chemical composition is 10-(N-methyl-3-piperidymethyl)-phenothiazine; it is dispensed as the hydrochloride monohydrate in tablets and as the acetate in ampoules. Each tablet contains the equivalent of 25 mg. free base, and each ampoule the equivalent of 50 mg.

The drugs in this group act centrally on the nervous system, modifying autonomic function, the action of the anterior pituitary, the reticular formation in the nervous system, and the balance of the enzyme systems of the brain. In animals conditioned reflexes are suppressed in varying degrees by different members of the group. Potentiation of anaesthetics and analgesics were the first actions turned to practical account; wakeful calming in excited mental patients, and substantial improvement in an unpredictable few are now the most important.

Chlorpromazine has been longest used and is the member of the phenothiazine group about which most is known. Pecazine resembles it in action but differs in the following ways: it is euphoriant, whereas chlorpromazine dulls the emotions; it inhibits sympathetic-like effects less, so that hypotension is less troublesome; it produces Parkinsonism and jaundice less often and convulsions more often than chlorpromazine. It seems to be less effective therapeutically than chlorpromazine in the psychiatric conditions for which the latter is commonly given.

Pecazine is worth trying in cases of psychosis displaying excitement, aggressiveness, restlessness, destructiveness, and impulsiveness, particularly in acute schizophrenia and mania. The dose usually prescribed is 300 mg. daily. In chronic schizophrenia, where the likelihood of remission is much less, doses up to 900 mg. daily have been given. Toxic complications have then resulted more often, but, as with many of the new pharmacological remedies, the patient has occasionally shown greater improvement than could have been expected from other measures or from none. Patients in this class who have not improved with chlorpromazine sometimes respond when pecazine is administered. About one-fifth of those chronic schizophrenics who have improved with pecazine will relapse when the drug is stopped. In treating the restlessness of senile dements and mental defectives, and in cases of delirium, pecazine does not seem to have any advantage over other drugs.

Pecazine should not be given to patients in coma or under the influence of barbiturates, narcotics, or alcohol. The frequency of side-effects and the poor evidence of its effect in mild and moderate psychiatric disorders appear to make it unsuitable for use in general practice. It is not beneficial to patients suffering from depression.

The side-effects occurring frequently are dizziness, dryness of mouth, paralysis of visual accommodation, and constipation. Slurred speech and hypotension are less common, while jaundice, Parkinsonism, epileptic fits, leucopenia, and agranulocytosis are rare complications. Of the last, however, fatal cases have been reported.

The administration of chlorpromazine and pecazine together produces fewer side-effects than an equivalent dose of either drug singly. A few patients who have not improved with either drug alone have responded when they were administered together.

N.H.S. basic price: tabs. 25 mg., 500 for 50s.; tabs. 100 mg., 500 for 180s.; amps., 10×2 ml., for 8s. 4d.; 50×2 ml., for 37s. 6d.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

B.C.G. Vaccination

SIR,—Lest your readers should be left with the impression that the 17 authors of the paper entitled "The Case Against B.C.G." (*Journal*, June 6, p. 1423) speak with the voice of America, I beg leave to quote other pronouncements on B.C.G. vaccination from the United States.

The American Trudeau Society (the medical section of the National Tuberculosis Association) in a statement made in 1949,[1] and reaffirmed since, recommends B.C.G. for medical personnel exposed to tuberculosis, individuals exposed to infectious tuberculosis in the home, patients and employees in mental hospitals, prisons, and other custodial institutions in whom the incidence of tuberculosis is known to be high, and children and adults considered to have inferior resistance and living in communities with an unusually high tuberculosis mortality rate.

The Medical Advisory Committee of Research Foundation[2] in 1957 called for an extension of B.C.G. vaccination in the United States and quoted the managing director of the National Tuberculosis Association as saying, "I believe the time is overdue when all individuals interested in tuberculosis control should make a strong effort to see that B.C.G. is used as widely as possible within the framework of the American Trudeau Society's statement."

It is relevant also to refer to the report[3] of the Ad Hoc Advisory Committee on B.C.G. to the Surgeon-General of the United States Public Health Service, published in 1957. This report is ignored by the 17. There was unanimous agreement that B.C.G. confers some protection against tuberculosis, and the committee expressed the opinion that its use should be determined by local conditions. While not recommending vaccination on a large scale (in the United States), the committee proposed as suitable groups to be vaccinated those mentioned in the American Trudeau Society's statement[1] quoted above.

I should also like to refer to the 1958 conference of the Tuberculosis and Health Association of Greater New York at which Dr. J. Holm, chief of the Tuberculosis Section of the World Health Organization (1959), said, "I wish to emphasize that we in W.H.O. have no doubt about the protective effect of a correctly performed vaccination, and that we consider B.C.G. vaccination just as important for our tuberculosis control program as the use of anti-tuberculous drugs."

It is thus clear that the 17 are not speaking for the United States in this matter. Their case against B.C.G. is not supported by any fresh evidence nor by the personal experience of any of the authors; they have been content to review some of the literature and arrive at conclusions based on their individual or combined opinions of other people's opinions and work.

Complacency about the tuberculosis situation in some parts of the United States may be justified by such findings as a reactor rate of not more than 2 to 3% in some rural areas, but something very different must be said of Chicago, for example, where in an editorial article in the *Journal of the American Medical Association*[4] it was stated that 11% of elementary and 31% of high school pupils were reactors. These are certainly not the over-forties mentioned in the paper, nor are they a legacy of the distant past. Indeed, there must be as much tuberculous infection circulating in Chicago as, say, in Belfast.

A remarkable headline in the paper is that reading "Immediate Danger of Natural Primary Infection Over-emphasized." A series[3] of 813 infected children is quoted of whom *only 11 died of tuberculosis and 11 developed chronic disease* (the italics are mine). In another series[4] of 2,979 reactors 137 developed chronic tuberculosis. Thus among 3,810 reactor children 159 developed "the chronic reinfection (clinical) type of tuberculosis which causes so much illness and death." The 17 emphasize the 3,651 who had escaped illness so far, but if B.C.G. had been used before natural infection a still larger number of children would have escaped illness.

It is relevant in this connexion to quote Miller *et al.*,[7] who examined the records of 313 children in Newcastle upon Tyne known to have been infected in the first two years of life. 150 were admitted to hospital ill and 62 were admitted during observation as contacts. The presenting illnesses in the 150 included tuberculous meningitis in 48 and pulmonary disease, including miliary tuberculosis, in 56. These were not the backlog of two decades ago.

Professor J. A. Myers and his colleagues are highly to be commended for the steps they have taken to protect medical students and other hospital personnel from the occupational hazard of tuberculosis by introducing rigid contagious-disease technique where necessary, by patient-admission examination for tuberculosis, and pre-employment examinations of all personnel with subsequent periodic re-examination. There is a lesson here for those in charge of British medical schools and hospitals.

J. D. Aronson's now classical trial of B.C.G. vaccination in North American Indians[8] is dismissed because the diagnosis of tuberculosis was made too much on radiological evidence. It is not mentioned that 65 of 1,457 controls died of tuberculosis in the period of observation compared with 12 of 1,551 vaccinated persons. The finding in the interim report of the Tuberculosis Vaccines Clinical Trials Committee of the Medical Research Council[9] is discounted also, this time because the physicians concerned may have failed to differentiate between tuberculosis and *x*-ray shadows. It is not mentioned that 68% of the persons in whom tuberculosis was diagnosed by the standards of the trial were sufficiently ill to be taken off work for at least three months. This interim report covered two and a half years only, but further information has been made available by Hart *et al.*[10] They report no waning of protection up to at least four years. This added information does not appear to have reached the United States.

The question of the possible mutation of B.C.G. towards increased virulence is discussed. The subject should be kept always under review. It is, however, well known that bacteriologists are more concerned with progressive attenuation of the strain and its consequent failure as a protective vaccine. The work of Petroff *et al.*[11] in dissociating B.C.G. into harmless and pathogenic colonies is rightly mentioned, but there should also have been mention of the failure of many other investigators to repeat his experiments with the same result—viz., the emergence of a strain which invariably produced progressive tuberculosis in guinea-pigs.—I am, etc.,

Whitehead, Co. Antrim. H. G. CALWELL.

REFERENCES

1. American Trudeau Society, *Amer. Rev. Tuberc.*, 1949, **60**, 681.
2. Medical Advisory Committee of Research Foundation, *J. Amer. med. Ass.*, 1957, **164**, 951.
3. Ad Hoc Advisory Committee on B.C.G., *Amer. Rev. Tuberc.*, 1957, **76**, 726.
4. *J. Amer. med. Ass.*, 1957, **164**, 974.
5. Torres, F. E., Myers, J. A., and Harrington, F. E., *Lancet*, 1944, **64**, 67.
6. Harrington, F. E., *The Evolution of Tuberculosis*, 1944, Division of Public Health, Minneapolis, Minnesota.
7. Miller, F. J. W., and McDougall, Ruth, *Brit. med. J.*, 1954, **2**, 846.
8. Aronson, J. D., Aronson, C. F., and Taylor, H. C., *A.M.A. Arch. intern. Med.*, 1958, **101**, 881.
9. *Brit. med. J.*, 1956, **1**, 413.
10. Hart, P. D'A., Pollock, T. M., and Sutherland, I., *Fortschr. Tuberk.-Forsch.*, 1957, **8**, 171, quoted in *Brit. med. J.*, 1958, **2**, 374.
11. Petroff, S. A., Brand, A., and Steenken, W., jun., *Amer. Rev. Tuberc.*, 1929, **20**, 275.

SIR,—After reading "The Case Against B.C.G." (*Journal*, June 6, p. 1423) and your excellent leading article "For and Against B.C.G." (p. 1460) I feel I must come in as a strong advocate for, and this is based on experience of B.C.G. for 10 years in the area of Britain with the highest incidence and mortality from 1900 to 1948. In Lewis B.C.G. was given to anyone wishing it after having been proved a non-reactor—the total number vaccinated is 6,000—3,000 by intradermal injection and, since 1953, 3,000 by multiple puncture. Of these 6,000 only one has developed tuberculosis, while during the period 1949 to date 62 under the age of 25 years have been notified, and of these 42 were positive and 20 negative at school. The non-reactors refused B.C.G.

Within the last month the following four young females have been admitted for sanatorium treatment. (1) Aged 18: negative in 1950—positive 1953 after sister, who had also been negative in 1950, developed pulmonary tuberculosis with positive spit in 1952. Other sister had B.C.G. 1950. Patient has bilateral cavitating disease with positive spit. (2) Aged 24: negative in 1950, 1952, 1953, left school non-reacting. Now has bilateral cavitating disease with positive spit. (3) Aged 12: negative 1953, 1955, positive 1957, violent positive 1959, tuberculous pericarditis. Her three older sisters had B.C.G. in 1950. (4) Aged 17: positive 1949 and on frequent occasions since; acute haemoptysis June, 1959.

With 18% of school entrants giving a positive tuberculin reaction in 1949–50 it should be evident that the risk of contracting tuberculosis was extremely great. The B.C.G. vaccinated ran as much risk as the non-vaccinated.

In Lewis, among the 3,000 given 0.1 mg./ml. by intradermal route, only three developed axillary adenitis with breaking down of the glands. Because of long delayed healing ulcers an attempt was made in 1953 to try multiple puncture after concentration of the Danish vaccine. In many cases this gave excellent results, with allergy still persisting, but for the majority the positive reaction disappeared after one year. In 1956 Glaxo, on request, produced a freeze-dried vaccine, 25 mg./ml., and used at 50 mg./ml., which gave consistent results, and these are more lasting. Presently I am engaged on the survey of close on 10,000 persons, tuberculin-tested and B.C.G.-vaccinated where necessary.—I am, etc.,

Stornoway. R. S. DOIG.

Jejunal Diverticulosis with Megaloblastic Anaemia

SIR,—I read with great interest and admiration the paper (*Journal*, July 18, p. 58) by Dr. G. Watkinson *et al.* on a case of massive jejunal diverticulosis with steatorrhoea and megaloblastic anaemia improved by excision of diverticula. In addition to the other evidence produced, the cure of the anaemia by resection of the affected gut seems to be conclusive proof that the megaloblastic anaemia is secondary to the disordered bowel function with added infection.

It may be of interest to report that the patient whom I originally showed at the clinical section of the Royal

Society of Medicine in 1949[1] with jejunal diverticulosis, fatty stools and hypoproteinaemia subsequently developed a megaloblastic anaemia with signs of subacute degeneration of the cord. The marrow was kindly examined for me by Dr. J. McSorley. The anaemia did not respond to folic acid but did show some partial response to chlortetracycline and complete response to vitamin B_{12}. The patient was followed up for about three years with continued treatment with B_{12}, but has now been lost sight of.

In my case free hydrochloric acid was present in the gastric juices after histamine stimulation, and therefore the megaloblastic anaemia and cord degeneration could not be due to concomitant Addisonian anaemia. It would thus seem that the total number of cases of jejunal diverticulosis with megaloblastic anaemia reported is now nineteen.—I am, etc.,

Whittington Hospital, London, N.19. E. MONTUSCHI.

REFERENCE

[1] Montuschi, E., *Proc. roy. Soc. Med.*, 1949, **42**, 868.

Telling the Cancer Patient

SIR,—The discussion on this subject should continue since it is important and no doubt it will influence the view of the younger generation of doctors. The letter of Dr. Hilda Swinburne-Jones (*Journal*, May 23, p. 1352) is most humane.

After over 45 years in practice I reflect that there are many reasons why no patient should be told that they have cancer. The effect is that from then onwards it is the first thought that will enter their minds every morning when they wake. I well remember a patient who was told that she had inoperable cancer and would live only a few months. She returned home and soon showed signs of delusional insanity, falling out with her kind relations and ending her life in misery.

How well I remember another woman who came with large lumps under her scalp which *x*-ray examination showed to be secondary deposits in bone. She had had a breast removed 25 years ago which her sister knew was for a carcinoma but the patient did not. She enjoyed 25 years of happy, useful life, but might not if she had been told.

Finally, doctors are not always right in their diagnosis: sometimes everything points to cancer and it is not so. I remember a case in which laparotomy disclosed what appeared to be a massive growth in the stomach with secondary glands in transverse fissure of liver. Three competent doctors diagnosed cancer and a hopeless prognosis was given to the relations; in spite of this the patient made an uneventful recovery and died of a stroke some six years later. Said a relation to the surgeon, "I admire your treatment but not your powers of diagnosis." In all events, if we cannot cure let us be kind.—I am, etc.,

Colwyn Bay. A. NORMAN LEEMING.

Inhibition of Lactation

SIR,—Your annotation on the inhibition of lactation (*Journal*, July 25, p. 96) draws attention to further evidence in support of the new concept that oestrogens do not actually suppress lactation but merely inhibit the consequent onset of breast engorgement. I believe this idea could be projected further into the field of prophylaxis, especially now that one single injection has been shown to be successful with no undesirable side-effects. The occurrence of mastitis in a lying-in ward—or even neonatal infection (since this is often the source of breast sepsis)—might constitute an indication for the prophylactic administration of an injection of such preparation as "primodian depot" to all mothers in that ward. Moreover, breast engorgement is not an uncommon complication of lactation. Perhaps its incidence could be diminished by the same prophylactic injection given routinely at all confinements.—I am, etc.,

Liverpool, 9. A. P. CAMILLERI.

Haemarthrosis

SIR,—On reading Dr. John Earle's letter (*Journal*, July 4, p. 20) I was reminded of a case of scurvy in this practice which I think is worthy of record, primarily on account of its unusual onset, and also because of its rather "story with a moral" type of aetiology.

A married woman, aged 43, had been attending the surgery for about four months complaining of pain with tenderness over the medial condyle of the left femur. She also had vague pains in the right ankle and leg, not so constant or well localized as in the other. *X*-rays showed no abnormality; symptomatic treatment including injections of hydrocortisone produced no relief. Then one day the right leg became oedematous and painful from ankle to mid-thigh. A thorough clinical examination revealed nothing except that she was of a very sallow, almost yellow, complexion and had a perifollicular hyperkeratosis on both lower legs; there was a trace of albumin in the urine. She was sent to bed for one week and then was allowed up, when a moderate-sized ecchymosis appeared on the posterior aspect of the right thigh, and clinical evidence of anaemia became manifest. Blood count: red cells, 3.7 millions; Hb, 75%; white cells, 6,000; P.C.V., 27; platelets, 230,000. Vitamin C excretion test=0.0103 mg.% (normal 3–5 mg.%). Treatment with massive doses of ascorbic acid produced rapid improvement in well-being and in the anaemia, but the pain in the bones still persists, though in a diminished intensity.

On questioning the patient about her diet, it transpired that some eight years previously she had suffered a gastro-intestinal upset and had been told to abstain from green vegetables for a while, and in fact she had not eaten any since, because "'she was afraid they would upset her." She has since recommenced eating greens with no ill effects. The cause of the oedema gave rise to some speculation here, but it was eventually decided that an intramuscular ecchymosis had caused occlusion of the deep leg veins.—I am, etc.,

Ashton-in-Makerfield, Lancs. N. TREVOR BURNETT.

Chlorothiazide and Hydrochlorothiazide

SIR,—Several recent articles have established the variations in dosage and effect of chlorothiazide and hydrochlorothiazide, but these results have not been equated in terms of the more familiar mersalyl. My series of 11 cases was studied in the manner described by Drs. C. W. H. Havard and J. C. B. Fenton (*Journal*, June 20, p. 1560), except that a week was allowed for the patients to settle; thereafter mersalyl, chlorothiazide, and hydrochlorothiazide were given in a differing order on alternate days with the initial one being repeated as further control at the end of the series where possible. The dose of chlorothiazide was kept at the maximum level of 1 g. twice daily, but dosage of the other two varied. Of the patients, who were maintained on a

salt-poor diet (17 mEq sodium/day), eight suffered from mild congestive failure with oedema, two had fluid retention due to steroid therapy, and one had Laennec's portal cirrhosis. Though individual variation was marked, it was clear that 75 mg. hydrochlorothiazide twice a day produced an excretion of water and electrolytes in 24 hours similar to the maximum diuretic dose of chlorothiazide. It is, however, worth recording that 2 ml. mersalyl usually produced a much larger volume of urine with a lesser concentration of sodium and potassium even when given at the end of the course, not uncommonly doubling the diuresis induced by the other compounds.

In rural and highland areas an oral diuretic is of great value, but as mersalyl so often causes a greater diuresis without danger of hypokalaemia this established favourite should not be forgotten or overlooked. A greater margin of safety is necessary if the newer compounds are to displace the older. This could presumably be established if (1) it is adequate to give a chlorothiazide along with the supplement, in spite of the demonstration by Drs. W. J. Poznanski and B. W. Cromie (*Journal*, June 20, p. 1553) that they are best given at different periods; (2) the problem of individual variation is met; and (3) the more potent hydrated form can be given with potassium chloride in one tablet of reasonable size.

Ciba Laboratories Ltd. kindly supplied the "esidrex" hydrochlorothiazide.—I am, etc.,

Inverness. RAE LL. LYON.

Purpura in Kwashiorkor

SIR,—I was much interested in Drs. E. Kahn and H. Stein's informative paper (*Journal*, July 18, p. 66). I do not wish to encroach too much on your valuable space, but I cannot help thinking that the criteria of a syndrome like purpura ought to be observed.

The authors describe 23 severely malnourished children suffering from "purpura." All had normal clotting times. Only two of them had prolonged bleeding times, thrombocytopenia and megakaryocytopenia, which in one of them appeared to be due to chloramphenicol toxicity. 70% of the patients were found to be suffering from tuberculous and salmonella infections. The relationship of these infections to purpura-like changes has been well known for a long time even in the absence of overt malnutrition. But why to describe purpura-like spots as purpura when haematological changes, including bleeding, were totally absent?

Similar purpura-like spots in connexion with protein malnutrition were described in such different parts of the world as Tunis,[1] Colombia,[2] and India.[3] In most of these cases bleeding, clotting, and prothrombin times were normal, and in Tunis the spots could not be prevented by administration of vitamin K and vitamin C. In one of my cases of secondary protein malnutrition syndrome in adults[4] punctate purpura-like spots and long striae with pinkish discoloration covered the greater part of the body, but no haematological changes indicating purpura could be detected, nor were these changes influenced by massive doses of vitamins, blood transfusion, or by any other treatment. These purpura-like spots and pinkish discoloration were authoritatively discussed by Gopalan[3] under the heading of cutaneous changes in protein malnutrition.

As long as protein malnutrition was diagnosed only in backward countries with no laboratory facilities the term "purpura" for these pink spots had to be accepted. In my opinion purpura-like spots fully covers the description of the authors; it does not imply non-existent haematological changes, and helps to avoid confusion about a syndrome which is now well defined and may be encountered and diagnosed all over the world.—I am, etc.,

London, W.1. Z. A. LEITNER.

REFERENCES

1. Caruana, M., Hamza, B., and Ghilebs, H., *Tunis. méd.*, 1953, **41**, 265.
2. Torres Umana, C., *Estudio sobre Edema distrofico*, 1953. Bogota.
3. Gopalan, C., in *Protein Malnutrition*, 1955, edited by J. C. Waterlow, p. 165. Cambridge.
4. Leitner, Z. A., *Lancet*, 1958, **2**, 504.

The Occasional Obstetrician

SIR,—I hope the article entitled "The Occasional Obstetrician" by Professor A. M. Claye (*Journal*, August 1, p. 104) will promote action in this chaotic position. Like my contemporaries, I set out six years ago, armed with the D.Obst.R.C.O.G., to carry my theories of ideal domiciliary care into operation. I now have to admit reluctantly that compromise is usually necessary and the ideal unattainable.

The chief enemy is time. It is impossible to book any case in a single-handed practice without the gnawing anxiety, "Will this case require my presence for an hour or more, when I might have to leave a crowded waiting-room stranded?" It is not conducive to an easy mind to know there will be much difficulty in finding time for anything more than a short visit during labour, unless it is a night case—then one feels like a wet rag by the evening surgery following. Another enemy is the multiplicity of antenatal care offered the patient, leading to many more attendances than reasonable, and varied advice. Another problem is the attitude of the midwife to the doctor. We want to work as a united team for the patient's welfare, but it can seldom be arranged that the midwife and doctor even do the antenatal care at the same time, never mind give the same opinion. The atmosphere between doctor and midwife is often fraught with emotions of underlying criticism and resentment. The midwives taunt us with lack of practice, yet they get indignant if we want to deliver a normal case.

It seems to me the answer lies in the appointment of a new type of occasional obstetrician, one who would do nothing else but domiciliary midwifery, and who would be appointed to an area and be responsible for supervising all home deliveries. Why not turn the present local authority antenatal officers into this? Then no one would be cut out, as their work is really rather unnecessary nowadays as it stands. This new type of registrar-grade obstetrician should be present at the delivery if requested by the G.P., and in any case should be the referee in difficult problems. Of course it would be too much to ask that he should also have access to the specialist maternity hospital of the area and have the power to supervise himself any case removed there owing to a complication in labour.

This is the type of scheme our patients would welcome, and it could surely not be called extravagant. What about the College of General Practitioners sponsoring it in a pioneer area? The desperate situation needs concrete action now.—I am, etc.,

Welling, Kent. DOREEN S. BALL.

Sterile Syringe Service for General Practitioners

SIR,—Central syringe services are accepted as the most satisfactory way to improve the sterilization of syringes.[1] In general practice the sterilization of syringes presents an even greater problem than in hospitals. It was mentioned by Dr. John Hunt[2] as one of the subjects to be taught by a college of general practitioners, and methods varying from boiling in oil to pressure cookers and conducted heat have been advocated. These may be necessary and efficient in small self-supporting units, but since central services have eased the work of our hospital departments there seems to be no reason why general practitioners and public health departments should not take advantage of them too.

Our hospital syringe service has been open to general practitioners for three months and is greatly appreciated by them, whilst causing little extra work to the department. It was designed to deal with up to 1,000 syringes a day, and is equipped with an infra-red sterilizer, drying ovens, a syringe washing machine and rinser, and a needle sharpener and ultrasonic washer. Syringes are issued in Nuffield aluminium containers with needle attached, packed in cardboard boxes of varying sizes, according to the requirements of the different wards or departments.

This system is easily adaptable to varying needs. Practitioners receive a box containing ten 2-ml., two 5-ml., and one 10-ml. syringes with needles attached. The most popular size of needle is No. 15, but syringes with different size needles are available, distinguished by coloured caps on the Nuffield container. A few spare needles in glass containers are supplied with each box, but are rarely used.

After use the boxes are returned to the centre and exchanged for new ones. Where it is more convenient, boxes can be exchanged at one of the outlying hospitals, but this is not encouraged, and the main stock is kept at the centre. Practitioners can have as many boxes as they like, and exchange them as often as necessary. The cost of the hospital service is 4½d. per syringe. This includes salaries and wages, electricity, washing materials, transport, and breakages. Since no additional staff or equipment was needed for the practitioner service, practitioners are only charged for breakages, and these have been remarkably low. The average breakage rate in the hospitals has been 0.8%, but for practitioners it was only 0.13%.

Up to the present 34 practitioners have taken advantage of the service, and use 1,060 syringes per month. This amounts to 6% of the total number issued, but more practitioners are still coming in, and a rise to 10% is expected. Public health departments will soon join the scheme, and estimate a need for 2–3,000 syringes per month for their clinics and district nurses. We believe that this scheme is a great success, and a good example for the advantages of co-operation between the three branches of the health service.—I am, etc.,

G. BEHR.

Central Pathological Laboratory,
Burnley.

REFERENCES

[1] Nuffield Provincial Hospitals Trust, 1958, *Present Sterilizing Practice in Six Hospitals*. London.
[2] Hunt, J., 1952, *Brit. med. J., Suppl.*, **1**, 335.

Peptic Ulcer in Africans

SIR,—We have read with considerable interest the annotation on peptic ulcer in Africans (*Journal*, June 6, p. 1462), as it has become obvious to us within the past year or two that this condition is by no means as uncommon in African patients in Southern Rhodesia as has been formerly supposed. During the past six months 35 peptic ulcers have been diagnosed radiologically in this hospital. Of these, 28 were duodenal ulcers and 7 gastric. This is in marked contrast to the experience of one of us, who cannot recall having seen more than one case of peptic ulcer in an African in this centre during the years 1949–54.

We have gained the impression that this sudden increase in the incidence of peptic ulcer may be more real than apparent. Although reasonably efficient interpreters have been available to facilitate history-taking for a number of years, it has only been during the recent past that patients have been referred in increasing numbers for radiological examination on the basis that symptoms and clinical signs have suggested the presence of a peptic ulcer. Although diagnostic facilities have improved recently, and this undoubtedly accounts for some of the increase, we feel that it could not possibly account for the total observed increase in incidence. This opinion is strengthened by the fact that approximately 35% of cases referred for barium meals during the past six months—for whatever reason—have had peptic ulcers demonstrated radiologically. Any doubtful cases have been excluded from the numbers quoted above.

We are unable to explain the above phenomenon at present, but are in the process of undertaking a detailed survey of peptic ulcer patients admitted to this hospital, in the hope of helping to clarify the epidemiological aspects of this interesting phenomenon. It may well be that more modern standards of living are a potent aetiological factor. It is interesting to note that gastric carcinoma is also being diagnosed with increasing frequency in this hospital, and is perhaps not as rare as has been recently reported.[1]—We are, etc.,

B. J. BALDACHIN.
P. E. S. PALMER.

Mpilo African Hospital,
Bulawayo.

REFERENCE

[1] Clemmeson, J., *Brit. med. J.*, 1958, **2**, 42.

SIR,—The annotation on this subject in your issue of June 6 (p. 1462) calls for a few comments. The term "African" has no scientific meaning unless it is supplemented by information about environment both geographical and social. Thus the Yoruba of the tropical forest of southern Nigeria is a different African from the Hausa of the semi-arid northern part of that country, and the southern lawyer or politician a different one from the little man on his cassava farm a mile or less away. You say that M. Ellis[1] performed "only" 32 operations for ulcer per year at Lagos. You do not say how many operations for other major conditions he performed. Over the past five years I have performed a similar number of thoracoplasties annually. Does that mean that there is only little pulmonary tuberculosis about? Again, there are only very few operations for breast cancer. Yet we see this condition weekly in our out-patient department. The women just do not consent to amputation, and, in any case, present too late.

Professor Davidson's[2] overall impressions were gained on a journey which missed out West African countries. We would have told him plenty about the abundance of ulcer. He went up the East coast. Many of the ulcers seen in southern Nigeria do not require radiology for diagnosis. They have produced signs of stenosis which cannot be missed by first-year clinical students (and are, in fact, not missed by them). Ulcer surgery at Ibadan got well under way years before a radiologist joined us. The active ulcer, too, is quickly recognized provided one is free from impressions and prejudices about their extreme rarity in "Africa."

I think you are right in stressing the importance of variations in eating habits in the pathogenesis of ulcer. But you go on to say that improving educational and living standards are perhaps accompanied by an increasing ulcer tendency. As far as southern Nigeria is concerned this suggestion is contrary to fact. It is the unemancipated and poor little man who has the ulcer, like his counterpart in India, a fact not overlooked by Ellis, stressed again by me at the 1957 Congress of the International Society for Geographical Pathology[3] in Paris, and also suggested by Raper[4] from East Africa. The concept of ulcer as a disease of "civilization" does not fit the bill in some tropical regions and should now disappear from modern publications.

In conclusion, Sir, let me once more stress the need for abandoning generalizations and impressions about Africans and also about peptic ulcer, and let us tell each other what we really know, or think we know, even if it is confined to a small corner of the globe. Such information can then be co-ordinated and the result will make sense.—I am, etc.,

University College,
Ibadan, Nigeria. PETER KONSTAM.

REFERENCES

[1] Ellis, M., *Brit. J. Surg.*, 1948, **36**, 60.
[2] Davidson, L. S. P., *Lancet*, 1954, **1**, 614.
[3] Konstam, P. G., *Schweiz. Z. allg. Path.*, 1958, **21**, 229.
[4] Raper, A. B., *Trans. roy. Soc. trop. Med. Hyg.*, 1958, **52**, 535.

Multiplication of Trade Names

SIR,—I always read the literature from the pharmaceutical houses and I take notice of what their representatives tell me. Then I apply my mind to clinical applications. My task is becoming increasingly difficult because of the everlasting multiplication of trade names, and I think both the medical profession and the pharmaceutical industry are open to great criticism for this widespread confusion.

There has recently been introduced a drug called dexamethasone and the medical journals are freely advertising its merits and virtues. In fact, it is not all that good, and it has many of the disadvantages of its grandparent cortisone. What really exasperates me is the nomenclature. Here is a list of six different trade names for dexamethasone, with the maker's name: "millicorten" (Ciba); "decadron" (Merck); "oradexon" (Organon); "dexa-cortisyl" (Roussel); "dextelan" (Glaxo); "deronil" (Schering). The same confusion is prevalent in most other branches of modern therapy.—I am, etc.,

Peterborough. G. F. WALKER.

Adoption Act

SIR,—As one who also has to deal with a considerable number of adoptions, but from the venereological angle, I would hasten to tell Dr. Alan S. Ogden (*Journal*, August 1, p. 122) that the Adoption Regulations, 1959, are very far from being "another example of ill-conceived and ill-informed encroachment upon the liberty of the individual."

Dr. Ogden asserts that "congenital syphilis is practically unknown." That it may become so is one of the goals of all venereologists, and, as a result of the great work of the late Dr. Nabarro and others, it is perhaps within sight, but Ministry of Health official figures for the past four quarters show 16 notifications of congenital syphilis under 1 year and 400 over 1 year. How many more there may be undetected or not reported is anybody's guess.

"Every mother has a W.R. during pregnancy." I wish they did; certainly the position is much better than it was even five years ago, but too many still elude us.

"Serologically positive mothers are very rare." This is certainly not the experience of the V.D. clinician, to whom these by no means rare patients are referred, nor of the antenatal clinics and doctors who refer them. Until such time as Dr. Ogden's "practically unknown" and "very rare" become reality, it is to be hoped that the Adoption Regulations will continue to be strictly enforced.

Those of us who all too frequently are called upon to give comfort and encouragement to those overwhelmed by dismay and misery on the sudden revelation, early or late, of congenital syphilis, will appreciate best the continuing need for early serological tests.—I am, etc.,

London, W.1. W. H. DICKINSON PRIEST.

Anaesthesia for Bronchoscopy

SIR,—With reference to the article by Dr. S. Gupta (*Journal*, March 14, p. 695) and the letter from Dr. I. A. Kellock (May 9, p. 1241), we would like to mention that in this department we use lignocaine 2% for local anaesthesia and propyliodone aqueous as the contrast agent for bronchograms. The following is the procedure adopted now. Skin sensitivity tests are done for lignocaine and iodine, even though the rationale of these is disputed. General anaesthesia is never given for bronchoscopy, as we take advantage of the co-operation of the patients during aspirations and instillations. Premedication is adjusted according to the extent of the lung lesions and the weight. Morphia is avoided in the presence of wheezing and pethidine substituted. Atropine 1/100 gr. is given subcutaneously an hour before instillation of dionosil. Eight drops of adrenaline hydrochloride 1 in 1,000 are added to one ounce (28 ml.) of 2% lignocaine solution. After the initial spray of the throat 1 ml. of lignocaine solution is syringed into the larynx twice, with an interval of twenty minutes. We aim at only laryngeal anaesthesia, as the bronchial mucosa is thought to be insensitive. Only one side is explored at a time for fear of broncho-spasm setting in. Dihydrostreptomycin 1 g. and procaine penicillin 500,000 units mixed is instilled into the bronchus after every bronchoscopy with no evidence of intolerance. Fortunately I have experienced no difficulties during the past four years in around 500 cases of bronchoscopies and in half this number of bronchograms. We, however, had anxieties during the earlier years, due probably to unadjusted doses of morphia and to the instillation of larger quantities of the local anaesthetics.—I am, etc.,

P. K. CHANDRASEKARAN.
Government Tuberculosis Sanatorium.
Madras, India.

Quarantine Outmoded

SIR,—While you were having your printing difficulties I received a letter from my daughter's school: "There is one case of German measles in the school. We are therefore in quarantine until August 3."

Is it not time that the school doctors agreed that small children ought to be exposed to mumps rather than protected from the disease, and that if possible all girls should be exposed to German measles before they leave school?—I am, etc.,

Oxford. G. W. PICKERING.

Inoculation Recording by Tattooing

SIR,—The article by Mr. N. C. Lake (*Journal*, August 8, p. 141) recommending the recording of inoculations by tattooing is an interesting one, but the siting of such a tattoo should be very carefully considered. In these days when reconstructive surgery is playing an ever increasing role in congenital deformities, burns, trauma, and malignant conditions of the head and neck, no site should be selected which may be used in the course of plastic surgery. The skin behind the ear should not be touched, as it is the best site for Wolfe grafts; the skin of the upper chest and abdomen is frequently used for tube pedicles destined for the face; and the arms and legs are constantly being used as donor sites for free grafts. Even the great toe should be left undisturbed, as it may well become a reconstructed thumb. As Mr. Lake suggests, the area just below the iliac crest appears to be the most suitable site, but any committee appointed to consider this project should have a plastic surgeon as one of its members. But meanwhile I hope a Sherlock Holmes will discover a method of tattooing with invisible ink.—I am, etc.,

Liverpool. L. B. SCOTT.

SIR,—Mr. N. C. Lake is to be congratulated on the ingenuity of his article on "inoculation recording by tattooing" (*Journal*, August 8, p. 141). While the method would be useful for indicating that a course of tetanus toxoid (3 doses) had been completed, it would be impracticable for records of reinforcing doses and dates. The date of the last injection of toxoid (primary course or reinforcement) enables a surgeon to decide whether antitoxin, or further toxoid, or neither, is indicated in an accident case.

The disk method (*Journal*, March 7, p. 640) would assist the personal record problem if it were taken up enthusiastically by administrative bodies as an adjunct to an official issue of cards. The lack of facilities for engraving the disks is the main difficulty at present, but it is not inconceivable that local authority clinics might install engraving machines. The set of three disks on a swivel, with much diverse information on the four internal surfaces, is liked by parents and is proving useful in practice for children of three years and upwards. There has been no defacement or loss in a small-scale experiment. Mr. Lake's fear that the disks might be discarded in course of time as a nuisance could well apply to those carried round the neck or in a wrist ornament. However, adaptability is one of the advantages of the disk method. Disks can readily be transferred to a key ring, or may be carried in a purse, wallet, or handbag. Indeed, I have kept a set (like a two-shilling piece in size and weight) for over six months loose in my pocket. The habit of carrying disks somewhere on the person can easily be formed, especially if encouraged by propaganda stressing the obvious advantages to the individual concerned.—I am, etc.,

Beckenham, Kent. H. J. PARISH.

Water Intoxication

SIR,—Dr. R. Emery's cases (*Journal*, August 15, p. 190) were vastly more serious and more definite than mine, but no doubt they were examples of the same condition. Mine were in colostomites, one of whom, I regret to say, was myself before I had learnt wisdom in the control of my stoma. We both got into trouble through over-enthusiastic washouts; we found that it took more and more fluid to ensure a thorough evacuation. As our colons got increasingly used to the distension they tolerated larger and larger volumes of water (yes; we did both use water rather than saline), until we were pumping in several gallons per washout; not all at once, of course, but about a quart (2.3 litres) at a time. When we had been doing this for a few months we started having epileptiform fits—major ones—perhaps about once a fortnight on the average. We ultimately connected the washouts and fits in our minds and gave the washouts up, after which neither of us had any more fits.

This sounds more conclusive than perhaps it was, because in these cases there must always be multiple factors, I suppose. Both of us were in a poor nutritional state and taking various medicaments for our diverticulitis and ulcerative colitis, respectively. However, there was no denying that we first started fits on huge washouts and stopped having fits when we stopped the washouts. I would say at least that our cases, reported at the time in the *Journal*, February 19, 1956, p. 398, were a warning against washouts, as distinct from enemas, in colostomy control.—I am, etc.,

Tonbridge, Kent. E. CLAYTON-JONES.

Influenza

SIR,—Dr. John Fry (*Journal*, August 8, p. 135) does us a great service with his reports on influenza and other epidemics, and one hesitates to criticize him when clinical impressions are all that one can offer as a counter to his own carefully documented observations. Nevertheless, I would challenge his remark that "a respiratory illness that is over in a few days is certainly not true influenza." I think that the answer to his mistake lies in the statement which follows, in which he includes analgesics as part of his routine treatment. Some time ago, working from first principles, I formed the theory that any treatment which suppressed the fever of virus infection would seriously impede the body's ability to overcome the disease. I noticed that during epidemics of influenza and the common cold patients often came complaining of persistent symptoms and that these people had almost invariably been taking analgesics continuously since the onset of the illness. Since that time I have persuaded patients with these conditions to do without the immediate benefits that aspirin and similar drugs can bring, in return for an assurance that their cure will be rapid and complete. I explain that it is not necessary or desirable to reduce the temperature, and that, on the contrary, they should try to get it up as high as possible with the aid of hot drinks, hot-water bottles, and blankets. Unfortunately I have no figures to demonstrate the success of this line of management, but I am certain that most patients make a complete recovery within a few days and that my complications rate does not begin to approach that of Dr. Fry.

I was relieved to see that Dr. Fry (? somewhat reluctantly), agrees that it may be desirable to treat all those over the age of 70 with prophylactic antibiotics. I cannot personally see why he should limit this advice to this age group. Surely it is reasonable to try to prevent complications, which occur in as many as 10% of a group of patients, and by this somewhat arbitrary standard all children up to the age of five and all adults over 50 with influenza should be so treated. The

expense factor should not be allowed to interfere with what is clinically desirable, and I can think of no other valid reason for withholding antibiotics. The whole matter is, however, of great interest and importance, and I hope that Dr. Fry's article will stimulate the discussion which it deserves.—I am, etc.,

Margate, Kent. M. CURWEN.

Transplantation of Foetal Tissues

SIR,—Our attention has been drawn to an article in the *Daily Express* on Saturday, August 1, purporting to describe some of the work on transplantation of foetal tissues done at this hospital.

As the only doctors at this hospital who have published any article on this subject (*Journal*, February 28, 1959, p. 575), we should like to dissociate ourselves entirely from what has been stated in the *Daily Express*. Much of the article is plainly inaccurate—e.g., no member of the staff here has, so far as I can ascertain, ever visited Dr. Niehans. No renal grafts have been performed, and to talk of revitalization is sheer moonshine.

None of the facts in the article was communicated by either of us to Mr. Pincher.—We are, etc.,

Royal Marsden Hospital, London, S.W.3. H. E. M. KAY. M. CONSTANDOULAKIS.

Anglo-German Medical Society

SIR,—Preliminary inquiries have shown that there is considerable interest among British doctors in the furtherance of Anglo-German relationships in the field of medical science and medical practice. A similar body of interested doctors exists in Germany and it has been decided to attempt the formation of an Anglo-German Medical Society, without prejudice to other international associations and with the possibility of affiliation as occasion arose. The object of the society would be, in the first instance, the promotion of visits and exchanges between British and German doctors engaged in all types of medical practice, teaching, and research. There are many other activities that could be undertaken by such a society, but space does not permit of their discussion here.

It has been found most opportune to hold the joint inaugural meeting of both the British and the German sections of the proposed society in London at 6.30 p.m. on September 9. Would any doctor who is interested in the formation of this society, and who has not been reached by previous circulars, please communicate with the second of the undersigned at the Department of Chemical Pathology, St. Mary's Hospital, London, W.2. —We are, etc.,

Dundee. W. WALKER.
London, W.2. E. KAWERAU.

POINTS FROM LETTERS

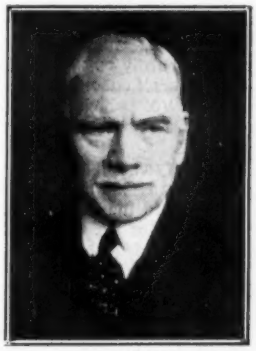
Portraits of Edward Lawrie and Sir Gerald Bomford

Dr. W. STANLEY SYKES (Morley, Leeds) writes: I am anxious to have a portrait of Edward Lawrie, born 1846, died at Hove, 1915. He was residency surgeon at Hyderabad. Also of Surgeon-Major Bomford, afterwards Sir Gerald Bomford, who took part in the Chloroform Commission. He was born 1851, died 1915. If anyone can lend me either, or both, of these, they will be photographed and returned.

Obituary

Sir ROBERT YOUNG, C.B.E., M.D., F.R.C.P.

A professional career extending well back into Victorian times is ended with the death, which took place in London on August 22, of Sir Robert Young, consulting physician to the Middlesex and Brompton Hospitals. He was a great physician, who attained the highest rank not only in professional achievement but in the esteem of his colleagues, his students, and his patients. Probably more than any man of his generation in this country he influenced the treatment of diseases of the lung. A former house officer of his at the Middlesex Hospital, Mr. T. Holmes Sellors, described him on his 80th birthday as the doyen of chest medicine for more than a quarter of a century.



[Walter Stoneman

Robert Arthur Young was born on November 6, 1871, the son of a Norfolk gentleman. He was educated at Westminster City School, from which he went on to King's College. He entered the Middlesex Hospital as a student in 1889, at a time when John Bland-Sutton, Essex Wynter, and William Hern, all of whom subsequently achieved exceptional distinction, were in junior posts on the staff. Those were days when the members of the staff, wearing frock coats and tall hats, arrived at the hospital in a brougham, a victoria, or a hansom cab: the days of gaslight or oil lamps; of a few privately owned telephones; of terra-cotta coloured aprons worn by surgeons in the operating theatre. In the school at the Middlesex there were no professors. The *x*-ray "department" consisted of a small-coil vacuum tube costing £14. The chief pathological tests were those on the urine, usually carried out in the wards by the house-physician or clinical clerk. Blood counts and bacteriological examinations were rare. The only special departments were for diseases of the throat and nose, the eye, and the skin, and for diseases of women and children, and, except for these two last, there were no special beds.

Young had a brilliant student career. He took his B.Sc. (university scholar in physiology) in 1891, and his M.B. (with first-class honours in medicine) in 1894. In the same year he became licentiate of the Society of Apothecaries. He proceeded M.D., London (worthy of gold medal) in 1895. In 1897 he became Member of the Royal College of Physicians. This was followed by the Fellowship eight years later. He completed his medical education in Vienna, though the word "completed" in this connexion is one he would never have applied to himself, for he was learning until the end of his life.

At the Middlesex he held various appointments, including those of house-physician, lecturer in physiology, and pharmacology, curator of the museum, and warden of the college. His association with the Middlesex and with Brompton as physician and senior physician continued throughout his life. What was called his first retirement—for many years of active work remained to him—took place in 1936, and afterwards he served as consulting physician. A new association with the Brompton arose with the coming of the National Health Service, when Sir Robert Young became the first chairman of the board of governors of the

HEALTH CENTER LIBRARY

Hospital for Diseases of the Chest as a result of the designation of Brompton and the London Chest Hospitals as a hospital group. Under his effective leadership many difficulties were overcome, and at the conclusion of his term of office he was able to see the two hospitals, each with its own independent tradition, working in harmony. He also had much to do with the development of the Institute of Diseases of the Chest—a centre devoted to postgraduate study in its widest sense. Other hospitals which had calls on his services were the City of London Lying-in Hospital; St. Saviour's Hospital, St. Pancras; King Edward VII's Sanatorium, Midhurst; Acton General Hospital; and St. Luke's Hostel for Clergy. He was also physician to the London Life Association.

Young's reputation as a chest physician soon went far beyond the group of hospitals with which he was associated. His Lumleian Lectures to the Royal College of Physicians in 1929 have been said to mark the beginning of modern British chest surgery. His scheme was a medical review of surgery of the chest. Young would have claimed that in thoracic work the division between medicine and surgery hardly exists. He had already delivered, five years earlier, the Lettsomian Lectures to the Medical Society of London (of which later he was Orator and President), taking as his subject the treatment of pulmonary tuberculosis. His Harveian Oration, in 1939, on the pulmonary circulation as it was understood before and after Harvey was another noteworthy contribution which this *Journal* had the privilege of publishing.

The list of his writings during the last 25 years of his life included such titles as "The influence of naso-oral sepsis on the lungs and gastro-intestinal tract"; "Medical aspects of thoracic surgery"; "Diagnosis and treatment of abscess of the lung"; "Treatment of pleurisy"; "Advances in the treatment of diseases of the respiratory system"; "New drugs and old remedies"; "Treatment of acute bronchitis"; "Prognosis in chronic bronchitis and emphysema"; "Spontaneous pneumothorax"; "Perspective and poise in practice"; "Modern therapeutics." In 1937 he was the author of the article "Diseases of the lung" in Price's *Textbook of Medicine*. His first essay in medical literature was as far back as 1897, when he translated from the German Arnold Brass's *Atlas of Human Histology*.

Sir Robert Young served as examiner in medicine, physiology, and materia medica to the Universities of Birmingham and Bristol and to the Conjoint Board of the Royal Colleges. He was formerly censor at the Royal College of Physicians. His counsel was much sought after in various advisory and administrative fields. He was vice-chairman of the standing Advisory Committee on Tuberculosis, and from 1944 onwards vice-chairman of the National Association for the Prevention of Tuberculosis, in whose *Bulletin* on his 80th birthday appeared some noteworthy tributes to him from his younger professional colleagues. It was at this time that he was called into consultation during what proved to be the last illness of George VI. He was the oldest of the nine doctors in attendance. In the British Medical Association Sir Robert Young served on a number of special committees. At the annual scientific meetings he first served as secretary of the Section of Physiology in 1898. Later he was twice vice-president of the Section of Tuberculosis, and he was president of the Section of Medicine at the Annual Meeting at Eastbourne in 1931.

Appointed C.B.E. in 1922, he was knighted in 1947. Two years ago the honorary freedom of the Society of Apothecaries was conferred on him, and earlier this year he was awarded the triennial gold medal of the Royal Society of Medicine.

Although suggesting in his manner the old-world physician, "R. A.," as he was affectionately known, entered into the spirit of the new times, taking up new techniques and testing the merits of new methods. He was one of the first to advocate the value of mass radiography, which, as he told the Commonwealth and Empire Health and Tuberculosis Conference in London in 1949, meant almost a revolution in tuberculosis investigation. But he would at times complain that many patients to-day were over-investigated and over-doctored, and with all his appreciation of new methods he insisted on the primary place of the old methods of inspection, palpation, percussion, and auscultation, remarking that, if only one method of examination were permitted, inspection should take precedence of all else.

If noisy controversy was the only way in which great reputations could be gained, Sir Robert Young would never have gained his. His strength lay in his quietness and modesty and unobtrusiveness. With him the bedside manner was not an assumed pose, but part of the man himself. He carried it not only into the ward, but into the class-room, the lecture theatre, and the medical society. His kindly and courteous approach to the patient set a standard for all his juniors. He made it evident that the patient mattered above all else. He never used unnecessary words, but he had a way, when he was brought into consultation, of putting everything into perspective.

As a teacher he was admirable. One of his students said that he never made a stinging comment, and he showed loyalty to the lowliest. He was an ideal guide on what he called a "voyage of clinical adventure." There were many stories current of the humorous twist he gave to his teaching. On one occasion he is said to have promised a house-physician some specially valuable advice on their last round together. The "build up" was considerable, but the advice when it came was, "Never miss your lunch." One characteristic remark of his is quoted by Dr. J. G. Scadding, who at the time was in charge of beds at Hammersmith Hospital. A few distinguished physicians who had recently retired from the active staffs of their hospitals were invited in turn to take over beds at Hammersmith and to conduct clinical teaching for periods of three months. When "R. A." took over the beds normally in Dr. Scadding's charge he said after one of his rounds, "The students seem a better lot this term. They don't ask so many questions I cannot answer."

Sir Robert Young had an expert's knowledge of and interest in other things beside medicine, and his home in Down Street, Mayfair, was a collector's treasure house. But the greatest joy in his life were his three grandchildren.

He had been a widower since 1944. A son, Mr. William Robert Young, is a solicitor.

G. E. B. writes: The death of Sir Robert Young will evoke tender and affectionate memories in the minds of his former hospital colleagues, registrars, house-physicians, and the numerous general practitioners in many parts of the world who have sought his help and advice. His patients will also remember the kindness, sympathy, and patience they received from him, which did so much to relieve their sufferings and allay their anxieties.

I first met "R. A.," as he was affectionately known to generations of Middlesex students, when, in 1910, he was assistant physician in charge of the children's department. I was soon attracted to him as a teacher and a physician. His diagnostic powers, based on observation, knowledge, and experience, had an overwhelming appeal for me. On his ward rounds he would deal with one case thoroughly, demonstrating how much information could be obtained from a careful history and a meticulous clinical examination.

One of his old students told me subsequently that "R. A." had taught him "bedside manners," for he always treated every patient in his wards with kindness, courtesy, and consideration.

As his assistant physician at Middlesex and Brompton I became more closely associated with him for a period of 17 years. I learned much from him of the art of medical writing, as together we produced the section on "Diseases of the Lungs" in Price's *Textbook of the Practice of Medicine* in all its editions. Writing the first edition was a big task, as "R. A." was so heavily committed to hospital and private work. I used to dine at his house one or two evenings a week, and about 9 p.m. we would settle down to two or three hours' work, interrupted by numerous telephone calls for "R. A." arranging more appointments. I also had the privilege of carrying on "R. A.'s" hospital and

private practice while he was on holiday, and the experience I gained was of inestimable value to me.

During the second world war "R. A." returned to Middlesex and demonstrated to the later generation of students, in what appeared an almost miraculous manner, how it is possible for the skilled clinician to find out what is the condition of the lungs without first consulting the *x*-ray films. Those were the days! "R.A." was always readily accessible, and the numerous honours he received did not render him puffed-up or off-hand. He was undoubtedly one of the very great physicians we have had at Middlesex and Brompton, standing in a class of his own. He established and maintained himself in Harley Street by his own efforts; he climbed to the pinnacle of success by a combination of genius and hard work; his fame and reputation became greater with each succeeding year of his career.

As his humble disciple I pay my last tribute to him; we all mourn the passing of a great physician—"let us now praise famous men."

A former house-physician writes: I spent one of the happiest six months of my life as H.P. to "R. A." at the Brompton. Dr. G. E. Beaumont was the other member of this remarkable firm. "R.A." never skimped the examination of a patient. If he had not got time to examine a new case thoroughly on his routine visit to the hospital he would come back the next day. The ceremony of the round was always the same. The H.P. had, of course, already examined the patient and penned in the usual symbols and shadings on the chest chart. "R. A." then did his examination, never omitting a single stage, never hurrying. If necessary the bed was moved so that the light fell evenly on the patient's chest. If there was much noise outside the window would be shut. The examination over, "R. A.," the sister of the ward, and the H.P. unhurriedly went to the table where the case sheet was ready for completion. A piece of blotting paper was placed over the H.P.'s chart, and "R. A." then filled in his findings on a duplicate. This done, the blotting paper was removed, and the two charts were carefully compared. "Oh! I see. You have found a cavity at that apex, have you? Perhaps we had better examine the patient again." It was a great object lesson. I shall never forget it.

His was the second opinion sought by other members of the staff. One day he was asked to see a difficult case by a physician who represented, so to say, progress in chest diseases. As soon as we were by the bedside he said: "Look at this *x* ray, R. A. It's most interesting." "R. A." waved it gently aside: "Do you mind if I see the patient first my dear X?" And, so it seemed, to the amazement of the brilliant Dr. X, "R. A." made a correct diagnosis before looking at the interesting *x*-ray film. "R. A." loved the Brompton and everything connected with it, and he communicated this, too, to his housemen, as he did so much else.

J. NORRIS WHYTE, M.D., D.P.H.

Dr. J. Norris Whyte, president of the Northern Ireland Branch of the British Medical Association, and consultant physician to the North of Ireland Tuberculosis Authority, died in the Musgrave Clinic, Belfast, on August 13. He was 53.

Joseph Norris Whyte was born in Londonderry on September 3, 1905. Educated at Foyle College, Londonderry, and the Queen's University of Belfast, he graduated M.B., B.Ch., B.A.O. in 1929, proceeding to the M.D. and taking the D.P.H. three years later. After holding resident appointments in the Royal Victoria Hospital, the Ulster Hospital for Children and Women, and Purdysburn Fever Hospital, Belfast, he became interested in tuberculosis, and after a period of residence in Forster Green Sanatorium he entered the Surrey County Sanatorium, Milford, first as an assistant medical officer and later as deputy medical superintendent. He then joined the tuberculosis service of the Lancashire County Council, first at High Carley Sanatorium, Ulverston, in 1936. In 1943, when the Ministry of Health offered a mass-radiography unit to Lancashire, Dr. G. Lissant Cox placed Norris Whyte in charge of this, the first local mass radiography unit for civilians in England. When the Belfast Corporation tuberculosis committee decided to open a mass-radiography centre in 1945, Norris Whyte was appointed director, and remained in that post until 1947, when the Northern Ireland Tuberculosis Authority was formed. He was then appointed Medical Superintendent of Whiteabbey Chest Hospital and the Orthopaedic Hospital at Greenisland. In 1951, with a reorganization of duties, he became consultant physician to one of the largest administrative areas of the Authority, but continued as senior physician at Whiteabbey Hospital. One of the pioneers in mass radiography, he was also one of the first to recognize and to welcome the advent of pulmonary surgery.

A most enthusiastic member of the British Medical Association, Dr. Norris Whyte was a most valuable member of Branch council. He was chairman of Belfast Division, 1953–5, and vice-president of the Northern Ireland Branch in 1956–7. It was a source of pride to him and of pleasure to his friends when in May, 1959, he was elected president of the Branch. He had been a member of the Tuberculosis Group Committee of the B.M.A. since 1950, and for two years he was a member of the Central Consultants and Specialists Committee. He was also a member of the British Tuberculosis Association, the Irish Tuberculosis Society, the Ulster Tuberculosis Association, and the Ulster Medical Society.

Norris Whyte was a warm-hearted man who loved his own home and who enjoyed the friendship of many. He took a very real delight not only in his work but in such social occasions as medical dinners and similar meetings. His flair for organization showed itself in the establishment of the Belfast mass-radiography unit, and in the affairs of the Association. He was that rare combination of a really sound clinician and a most competent administrator. It was probably because of his own inherent fair-mindedness that he was quick to rebel against any decision which he thought to be unjust, either to himself or to others. His genial presence and his wise counsel will long be missed.

He is survived by his widow and two sons.—R. M.

C. P. RHOADS, M.D., D.Sc.

Dr. C. P. Rhoads, scientific director of the Memorial Centre for Cancer and Allied Diseases in New York, director of the Sloan-Kettering Institute for Cancer Research, and professor of pathology in Cornell University Medical College, died suddenly on August 13 in his 62nd year. By his death the world of cancer research has lost a dynamic character, a great personality, and a remarkable judge of scientists. He was born in Springfield, Massachusetts, and he had many of the qualities in manner and appearance which one associates with New England.

Cornelius Packard Rhoads was trained at Bowdoin College in the State of Maine, where he took his A.B. in 1920, and at Harvard, where he graduated M.D. cum laude in 1924. At Harvard he was a class-mate of Charles Huggins, another outstanding cancer research worker. After working in the Peter Bent Brigham Hospital, Boston, and the Trudeau Sanatorium, New York City, he returned to Harvard medical school as instructor in pathology in 1926. He became an associate of the Rockefeller Institute for Medical Research in 1928, where he was in charge of the service for the study of haematological disorders from

1933 until 1939. During the last war he served in the U.S. Army as chief of the medical division of the Chemical Warfare Service. Some of the men who were his war-time associates subsequently joined him when the Sloan-Kettering Institute opened.

At the end of the war Rhoads's plans for a large cancer research institute to be situated in New York began to take shape, and with the help of Mr. Alfred P. Sloan, an industrial magnate, and Mr. Charles F. Kettering, an engineer who had invented the automobile self-starter, the institute started within the Memorial Hospital. This institute, which is adjacent to the wards of the Memorial Hospital and close to the Rockefeller Institute and Cornell University Medical Centre, was opened officially in 1948 with over 100 laboratories, with divisions of steroid metabolism, steroid biochemistry, physics, and biophysics, clinical investigation, protein chemistry, experimental chemotherapy, and experimental pathology. Divisions of experimental surgery and steroid biology were added later. Important contributions to scientific knowledge have been made in all the divisions. The institute has grown, and a short time ago a subsidiary laboratory was planned and has been built at Rye on Long Island Sound, with funds from the legacy of the late Donald S. Walker. It is sad that Rhoads did not live to be at the official opening of this new laboratory. He won many distinctions, including the Legion of Merit (U.S.) and the Walker Prize of the Royal College of Surgeons.

"Dusty," as Rhoads was often called, was always optimistic about solving the problems of cancer and had enormous drive and ability to plan and organize large undertakings. He married Katherine S. Bolman, who, with her quiet charm and dignity, did much to support the tremendous activities of her husband. The deepest sympathy will be widely felt for her. Until a few years ago Rhoads had been a keen yachtsman. He was interested in military matters and had considerable knowledge of American military history. The Sloan-Kettering Institute was his creation, but he was more than an organizer and collector of funds. He was a great friend and support of many younger investigators, and was able to inspire many to give of their best.—E. B.

A. RUSCOE CLARKE, M.B.E., M.B., F.R.C.S.

Mr. A. Ruscoe Clarke, surgeon to the Birmingham Accident Hospital, died suddenly at Dudley Road Hospital, Birmingham, on July 10. He was 51 years of age.

Alan Ruscoe Clarke was educated at Haileybury College and Guy's Hospital. Graduating M.B., B.S. in 1931, he was admitted F.R.C.S. in 1933. He had been a member of the surgical staff of the Birmingham Accident Hospital since 1947.

Mr. William Gissane writes: This is not the hour of our great sorrow. That time passed when Alan Ruscoe Clarke died suddenly but peacefully following his first cardiac illness. Now we pay homage to a man who lived his life to its full professional and scientific capacity. Ruscoe never wasted time.

At Guy's Hospital he won the Michael Harris anatomy prize, the Wooldridge physiology prize, and the general proficiency prize in 1928 and was *proxime accessit* for the Treasurer's gold medal in both surgery and medicine in the year of his graduation. Such was the beginning of his medical career. Then followed five years of successive appointments at Guy's Hospital. He combined these with clinical assistantships at the hospitals of Great Ormond Street, All Saints's, and St. Peter's, in London. During this period he found time to gain his Fellowship of the Royal College of Surgeons of England one month after his 25th birthday. Awarded a Leverhulme travelling fellowship in 1936, he journeyed to the U.S.A. and held appointments at the Peter Bent Brigham Hospital and the Harvard Medical School. It was in America that he first became actively engaged in medical research.

Returning to England in 1938, he held various appointments within the London County Council hospital service, notably as first assistant in surgery at the British Postgraduate Medical School at Hammersmith. There, during the air raids on London, he worked alongside a Medical Research Council team studying traumatic shock. Then followed his war service with the R.A.M.C. as a surgeon specialist, working mostly at casualty clearing stations. He was at the landings in Algiers, in the Tunisian campaign, North Africa, and Italy. He was appointed M.B.E. in 1943 after the Tunisian campaign.

I first met Ruscoe on January 1, 1947, when he was appointed to the full surgical staff of the Birmingham Accident Hospital. Here obviously was a man dedicated to the cause of the injured. Over the years that followed he was the most loyal and pleasant of hospital colleagues, full of humanity, understanding, and with a well-balanced enthusiasm. As a surgeon he quickly developed outstanding clinical and technical abilities. Interested in research from his earlier work, and in spite of very considerable clinical responsibilities, he somehow found time to develop a major research programme.

From his war experience he appreciated the need to learn more about haemorrhagic shock and the pattern of blood loss following injury. It was entirely on his initiative that research was started on these lines at the Birmingham Accident Hospital. During the years new research workers joined him to develop and extend the work. They were continually inspired by his powers of leadership and his considerable clinical experience. He was that rare combination of experienced clinician and research scientist. The work of this research team has built up a pattern of solid evidence based on Ruscoe Clarke's surveys of the Birmingham Accident Hospital records and on research work inspired and led by him.

In my view this evidence makes clear the urgent need to establish in this country a completely different tempo and quality of hospital treatment service for the proper care of the injured, particularly the severely injured. Based on these findings and other research, British surgery could give a much needed lead to other countries in the care of their injured. This, I know, was Ruscoe's ultimate goal.

The work to which he contributed so much will go on. That, too, is a measure of his stature. He was pre-eminently a team man, and he believed that no one was irreplaceable. We are now testing that belief to its limit. The Royal College of Surgeons of England honoured Ruscoe Clarke with the Arris and Gale lectureship in 1952. Many more and greater honours would have come to him had his life not ended at such an early age. His work will live in the literature of medicine, his memory in the hearts of all those who knew him well.

W. A. S. LAMBORN, O.B.E., M.R.C.P.

Dr. W. A. S. Lamborn, for many years medical entomologist to the Nyasaland Protectorate, died at Fort Johnston, Nyasaland, on March 6 after a long illness. He was 82 years of age.

William Alfred Stedwell Lamborn was born at Battle, Sussex, in 1877. From St. Mungo's College, Glasgow, he went on to the Middlesex Hospital to receive his clinical training, and qualified in 1899. Among the appointments he held after qualification were those of assistant medical officer at the Islington Infirmary and assistant medical officer at the County Asylum, Littlemore, Oxford. In 1905 he went to British Guiana as assistant medical officer at the Public Hospital in Georgetown, and two years later he went to Africa, first to Pietermaritzburg, in the Natal province, and then to Lagos, where for a time he was medical officer to the Nigeria Bitumen Corporation. Before the first world war he also visited the Federated Malay States, and he carried out a malarial survey for the Japanese Government.

Appointed entomologist to the Nigerian agriculture department in 1913, he was at one time travelling entomologist in East Africa under the Imperial Bureau of Entomology. He first went to Nyasaland in 1915, and soon became engaged in the campaign against sleeping sickness. During the first world war he served in German East Africa from 1917, being placed in charge of Tanga Hospital, and becoming the first civilian medical officer of health for Dar-es-Salaam. In 1918 he became a medical officer in Nyasaland, and in 1920 assistant medical entomologist in the Federated Malay States. In 1921 he returned to Nyasaland to assume the appointment of medical entomologist to the Government, and for this work he was appointed O.B.E. in 1930. In 1937 he was elected a member of the Royal College of Physicians of London. During the second world war he served in Kenya as a major in the R.A.M.C. A member of the British Medical Association for over fifty years, he was president of the Nyasaland Branch in 1937–8.

R. R. S. writes: I had the privilege of serving under Dr. W. A. S. Lamborn for the six weeks before he left Dar-es-Salaam, where he laid sound foundations for the "cleansing of the Augean stables," as he described the conditions then obtaining. He earned a world reputation for his researches on the insect-borne diseases of the tropics, and compiled the first catalogue of the insects of the Nyasaland Protectorate. He was offered a professorial chair of entomology, but because of his absorbing interest in field work he decided not to accept it. His many publications include papers on artificial breeding places for *Glossina morsitans*, the breeding of *Papilio dardanus* in Southern Nigeria, a report on trypanosomiasis in Lower Ruvuvu, and, after an official visit to Bagdad, a report on the haematophagous fly as a possible vector of Leishmania. Extremely modest about his outstanding scientific achievements and of a retiring nature, he was beloved by his friends and honoured by his colleagues. Sincere sympathy goes out to his only son, now living in Nyasaland, and to other members of his family.

C. L. I. writes: In 1918 it was my privilege to take over Tanga Hospital from Dr. W. A. S. Lamborn. For several weeks afterwards, and much to his pleasure, he made the medical officer's house his headquarters, to which he returned from time to time from his studies in the field. At that time he was keen on planting the pupae of flies parasitic on the tsetse fly in their breeding-grounds. These parasites he proposed to rear artificially. So the medical store at Tanga at that time contained captive insects of several kinds. The amiable qualities of this modest man of genius will be recalled by a decreasing band of his contemporaries who knew him, but in connexion with his original work on insect mimicry his name will be remembered as long as entomology continues to be studied as a science.

R. S. C. McDADE, M.B., B.Chir.

Dr. R. S. C. McDade, deputy medical superintendent of Broomfield Hospital, Chelmsford, died at his home there on June 4. He was 54 years of age.

Robert Sinclair Charles McDade was born in London of Ulster stock on January 20, 1905. He was truly a son of the manse, for his two grandfathers and, before taking up medicine, his own father were Nonconformist ministers. Educated at St. Paul's School, St. John's College, Cambridge, and St. Thomas's Hospital, he qualified in 1931, graduating M.B., B.Chir. two years later. Among the resident appointments he held was that of house-physician at the Brompton Hospital. Later, he was deputy medical superintendent of Colindale Hospital and then of High Wood Hospital, Brentwood, before he went to Broomfield Hospital in a similar capacity nearly 20 years ago.

W. L. Y. writes: In the decades between the two world wars work in sanatoria attracted a number of men who found great satisfaction in that field. It is difficult for the new generation with its panoply of modern drugs to realize how much such men, with their equally devoted nursing staff, managed to achieve. With methods now considered obsolete and with infinite pains and sustained attention to detail patients were coaxed back to health, often when the balance seemed heavily weighed against them. To this work Roy McDade dedicated himself with a singleness of purpose. Strict he might be, but his patients realized that to him their treatment was important above all else, that they too must put their shoulder to the wheel, but that they were fortunate indeed to do it under his direction. On his ward rounds he was meticulous. Time he disregarded; for it he substituted work, and however late the hour the familiar white-coated figure might be seen passing along the dim-lit hospital corridor to his consulting-room, where, oblivious to all else, with his *x*-ray films and view box, he would ponder his cases and write his thoughtful and voluminous notes on which future treatment would be based.

But in his rare leisure who more quick to see the flying shaft of wit and raise a gale of laughter? In the bleak February days of last winter, when so many of the staff were struck down by influenza, though his health must have been failing, he was unsparing in his care of them. He set a high standard for himself and was steadfast in maintaining it. The things he had tried and proved he clung to. To his colleagues he was unpretentious, yet he under-rated neither his profession nor his country, but scorned those who did, and he cherished his Victorian ideals of self-help, self-sacrifice, and service.

When the old order in the hospital is changing he has finished his course, and we can add of this old Pauline that he has fought a good fight and kept the faith. His memory is enshrined in the words of a surgical colleague, "Dear old Mac," and our sympathy goes out to his widow and his father, Dr. C. E. McDade.

J. D. SINCLAIR, O.B.E., M.R.C.S., L.R.C.P.

Dr. J. D. Sinclair, honorary consulting physician to the Darlington Memorial Hospital, died at Darlington on July 26. He was 85 years of age.

James Donald Sinclair was born on January 2, 1874, and studied medicine at Edinburgh University, where he was a demonstrator in the department of anatomy. He qualified M.R.C.S., L.R.C.P. in 1904, and then held the appointment of house-surgeon at Doncaster Royal Infirmary. In 1906 he settled in general practice at Darlington, where he remained for the rest of his life. He was honorary anaesthetist to the Darlington Memorial Hospital for some time and later became honorary radiologist and honorary physician. Always keenly interested in the welfare of children, he established a fund to finance the building of a children's wing at the hospital. For over forty years he was a lecturer and an examiner in the ambulance movement in Darlington, being lecturer to one railway class for more than thirty years. He was appointed O.B.E. in 1920 for his services during the first world war, when he was medical officer at the 6th Durham Voluntary Aid Hospital, Darlington. Appointed a Serving Brother of the Venerable Order of St. John of Jerusalem in 1946, he was promoted to Officer (Brother) six years later. A member of the Darlington town council for some years, he was deputy mayor of the borough in 1942. He was chairman of the Darlington Division of the British Medical Association from 1922 to 1925, and had served as honorary secretary of the local medical war committee.

D. I. R. writes: I knew Dr. J. D. Sinclair for most of the latter half of his life and for all my own, for he brought me into the world. The usual childish ailments occasioned visits which were eagerly awaited, for he had a wonderful way with a sick child. It seems particularly appropriate that the children's ward at the Darlington Memorial Hospital should bear his name. As the years passed I grew

to know him better as a family friend and adviser, and so came to appreciate the breadth of vision and the whole-hearted enthusiasm of which both he and his wife were able to give so richly in voluntary service to the public. His quiet, unassuming manner was none the less authoritative, and I am sure that few could have turned to him in vain for advice or help. Many of his qualities stemmed from a deep and abiding religious faith, and local church affairs were always near to his heart. Although he had several severe illnesses during the twenty years of his retirement, those years were nevertheless extremely active. For that reason there must be many who only knew him as an indefatigable worker for good causes; others, like myself, have reason to remember with gratitude and affection that he was, above all, a good doctor.

W. R. F. writes: By the death of Dr. J. D. Sinclair, Darlington has lost one of its most eminent citizens. His practice of his profession as a faithful, conscientious, and skilful doctor was enriched by his manifold interests and his concern for his fellow men. He touched life at many points, and what he touched he adorned. There are in Darlington few bodies or causes devoted to helping others in which he did not play a leading part. He dedicated his life in his profession to the service of others with complete devotion to God. In the Edinburgh medical mission he learned to relate his religion to the practice of his profession, and there also he met his wife and life-long companion. Men and women trusted him, and children loved him. He was singularly happy in his home life, and in his home he gave and received the same loyalty that marked all his public life.

R. C. L'ESTRANGE BURGES, M.B., B.Chir.

Dr. R. C. L'Estrange Burges, a well-known Birmingham general practitioner, died at the Queen Elizabeth Hospital, Birmingham, on July 31. He was 58 years of age.

Richard Charles L'Estrange Burges was born on November 25, 1900, the eldest son of the late Dr. F. A. L'Estrange Burges, a highly esteemed Birmingham general practitioner, and was educated at King Edward's School, Birmingham, Caius College, Cambridge, and the Birmingham medical school. He qualified in 1925, and three years later took the degrees of M.B., B.Chir. After holding the appointments of house-surgeon at the Queen's Hospital, Birmingham, and house-physician at the Birmingham General Hospital, he joined his father in practice. He took an active interest in local medical affairs and was chairman of the Birmingham Division of the B.M.A. in 1956–7, having previously represented his Division at a number of Meetings. A member of the Birmingham executive council from its inception, he was also vice-chairman of the Birmingham local medical committee from 1957 until his death.

Dr. H. W. Donovan writes: Dr. R. C. L'Estrange Burges inherited many of his athletic and intellectual qualities from his father, and from his mother he acquired his love of wild flowers which set him on a path leading to nation-wide distinction as a field botanist. He made a number of important contributions to its literature, was elected a Fellow of the Linnaean Society, and became chairman of the Birmingham Natural History Society. Always good at games, he played cricket and rugby football for his school, Rugby for his college at Cambridge, and later for the Old Edwardians and for the North Midlands. At tennis also he excelled, being a Warwickshire county player for several years and a regular player for the Edgbaston lawn tennis club, of which he was chairman for five years.

Dick Burges, greatly loved and admired both by his patients and by all who knew him, was primarily a good doctor. Brought up in the best traditions of medicine, he was jealous for the honour and good name of his profession. He was deeply interested in clinical work and also in industrial medicine. He found time to play a part in training members of the St. John Ambulance Brigade and was medical officer to his old school. A man of strong personality and wide interests, with a keen, forward-looking mind, he was a delightful companion with a great sense of honour, a lively and fearless debater, and a fount of wisdom in committee. He could be forthright in voicing his displeasure at cowardice or stupidity, but to those, and particularly the young, struggling to make the most of what talents they possessed, he was kind and gentle, a loyal helper, a wise counsellor, and a true friend.

To many in this city his death is a grievous personal loss and leaves a wide gap in many walks of life. From all these, deep and sincere sympathy goes out to his widow and their only son, Dr. D. C. L'Estrange Burges, who succeeds his father in practice, to carry on into the third generation a great family tradition.

Medico-Legal

HOSPITAL CLAIM AGAINST INSURERS

[From our Legal Correspondent]

On July 30 Mr. Justice Salmon, in a reserved judgment, refused to allow a claim made under Section 36 of the Road Traffic Act, 1930, by the Barnet Group Hospital Management Committee against the Eagle Star Insurance Company Ltd. (*The Times*, July 31).

By Section 36, insurers are directly responsible, in respect of policies issued under the Act, for paying expenses reasonably incurred by hospitals which provide treatment, whether as an in-patient or as an out-patient, to any person who has sustained injury arising out of the use of the insured vehicle on a road or in a place to which the public have the right of access. (This liability is additional to the liability of the insurer under section 16 (4) of the Road Traffic Act, 1934, to indemnify the assured against payments made in respect of emergency treatment given by medical practitioners or hospitals.) The liability under Section 36 of the 1930 Act is dependent on two conditions—*first*, that a payment is made (with or without an admission of liability) by the insurers in respect of the injury under the policy issued under the Act, and *secondly* that the treatment has been given to the knowledge of the insurers.

In the present case the hospital committee sued the insurers for expenses incurred in giving hospital treatment for injuries sustained in a road accident by a passenger in a car whose driver was insured with the defendant insurers.

The policy covered all liability required to be covered by the Act of 1930 and in addition covered liability to passengers in the insured's car. The insurers made a payment to the passenger in respect of his injuries. At the time of payment they did not know that he had received hospital treatment, but they did know this before the writ was issued.

On these facts, two points of law were decided in favour of the hospital and one against.

First, it was decided that a policy was a "policy issued under the Act" notwithstanding that it included cover beyond that made compulsory by the Act. The payment to the passenger was made under a cover not made compulsory by the Act, but it was nevertheless made by an authorized insurer under a policy issued under Part II of the Act, since the policy included the compulsory cover.

Secondly, it was decided that prima facie the passenger was clearly "any person" within the meaning of Section 36. To hold, as the defendants argued, that "any person" meant any person required to be covered by the Act would involve writing words into the Act which were not there. There was no reason why the provisions of the section, intended to protect hospitals, should be confined to persons compulsorily insured and exclude passengers.

However, the court decided also that it was compelled to follow the strict grammatical interpretation of the words of the section to the effect that, in order for any liability to fall upon the insurers in respect of hospital treatment, they must have knowledge of the treatment before making any payment to the injured third party. The defendants had argued that it was sufficient if the insurers knew of the treatment before the issue of the writ, as in this case, but this argument was rejected.

Clearly in view of this decision, if a hospital contemplates a claim against an insurance company under Section 36 of the Act of 1930. the hospital should ensure that the insurers do have knowledge of the treatment as early as possible.

Universities and Colleges

UNIVERSITY OF ST. ANDREWS

At a Graduation ceremonial on June 30 the following degrees were conferred:

M.D.—[1]H. B. Goodall (with Rutherford gold medal for thesis), [1]W. Shepherd, [2]W. B. Robertson, A. D. Forrest.

CH.M.—[1]G. Smith, [2]D. W. Blair.

M.B., CH.B.—[1]R. F. Macadam, [1]R. Plotkin, [2]P. D. Bewsher, [2]Helen B. Brodie, [2]K. G. Millar, Jane E. Anwan, J. N. Bell, A. Bertram, R. Y. Bishop, W. I. K. Bisset, A. W. Blair, J. R. Brown, A. J. Browne, M. R. Cassim, A. B. Chaloner, M. Dalton, Patricia A. Evans, R. Gillespie, H. J. Grycz, E. Hamburger, Jean B. G. Hamnett, D. G. Harries, J. M. Holt, T. H. D. Horsley, J. W. Innes, G. B. James, G. N. Jamieson, Celia M. Jenkinson, Marie G. Kellock, W. E. Kroutil, Gareth E. Leyshon, W. A. F. McAdam, Elizabeth A. Mackay, A. L. Macnair, M. Macphail, Christine A. Main, A. N. Munro, S. A. Nairn, J. E. Neehall, J. T. Robson, A. Saungsomboon, J. M. Small, Irene A. Smith, I. MacD. Strachan, I. Waheed, I. Wallace, F. G. Ward, I. H. Wishart.

[1]With honours. [2]With commendation.

UNIVERSITY OF BIRMINGHAM

The following degrees were conferred on June 22 and July 11:

CH.M.—D. J. Oakland.

PH.D.—*In the Faculty of Medicine:* D. A. Heath, M.D., W. M. McKernan, K. Aterman, M.D., M.R.C.P., D.C.H.

M.B., CH.B.—A. Rhodes (with second-class honours, and distinction in medicine, in forensic medicine and toxicology, and in social medicine), F. K. Wright (with second-class honours), R. Baker, J. W. Bland, B. A. Boughton, Joan M. Brown, R. M. Brown, Angela R. Buckley, Annie R. Burgess, S. W. Clarke (with distinction in paediatrics and child health), R. M. Clewlow, A. J. Cox, N. A. Dent, D. Donaldson, Mary S. Duncan, Judith Ellison, F. Farmer, R. M. Finch, D. M. Fleminz, Latita M. Fooks, D. Galliford, M. J. Gilbert, M. F. Grayson, L. H. Grove, A. W. Harris, B. Hill, J. B. Hollins, June M. Hunt, Susan P. Jones, T. T. Jones, S. C. Kennedy, N. G. Lambert, Bozena Z. Leoszke, Gillian K. M. McMullan, Jennifer P. Mansfield, A. B. Masters, J. H. Morris, J. F. Morris, J. T. Mucklow, R. W. Myers, C. D. Neal, P. Omo-Dare, J. C. E. Parkinson, B. G. S. Peach, J. E. Perrin, A. J. Perrons, J. R. Perry, W. R. Plimbley, Kathleen W. Raine, P. M. Rainsford, A. L. Revell, Anne L. Riffkin, P. Sadler, Phillida A. Sampson, Anne R. Schofield, B. J. Sealey, T. Shaw, J. R. Smethurst, A. G. E. Smith, Barbara G. Smith, C. S. Tyler, N. A. Ward, Romola I. Westwood, Janet A. Williams, P. M. Worrall, J. G. Wright.

(The degree of Ch.B. was conferred *in absentia* by special warrant on June 22 on all the above successful candidates for the degree of M.B. On July 11 the degree of Ph.D. was conferred, on K. Aterman, and the degree of M.B. on S. W. Clarke and J. H. Morris, all *in absentia*.)

Sir Arthur Thomson has been appointed representative of the University on the council of Malvern College.

The title of Honorary Lecturer has been given to the following: *Department of Pathology*, Dr. A. H. Cameron, consulting clinical pathologist, United Birmingham Hospitals, and University Clinical Lecturer in Pathology; *Department of Experimental Pathology*, Dr. C. N. D. Cruickshank, Assistant Director, Medical Research Council Unit for Experimental Pathology of the Skin, and University Research Fellow; *Department of Bacteriology*, Dr. K. B. Rogers, Consulting Clinical Pathologist, United Birmingham Hospitals, and University Clinical Lecturer in Pathology.

The title of University Research Fellow has been given to Dr. O. C. Forbes during the tenure of his award of Research Fellow sponsored by the Food Research and Toxicological Unit, or for the period of his stay in the University.

The board of governors at the United Birmingham Hospitals has granted honorary status to Dr. J. M. Bishop and Dr. P. C. Harris as honorary consultant physicians and to Dr. J. Butler, who resigned his appointment as Lecturer in Medicine on June 30, 1959, as honorary senior registrar.

The following appointments are announced: Dr. L. T. Clarke and Dr. B. L. S. Murtagh as part-time Lecturers in Anaesthetics from April 1, 1959, and Dr. A. J. Essex-Cater as part-time Lecturer in Child Welfare in the Department of Paediatrics and child Health from January 1, 1959.

Vital Statistics

Poliomyelitis in the U.S.A.

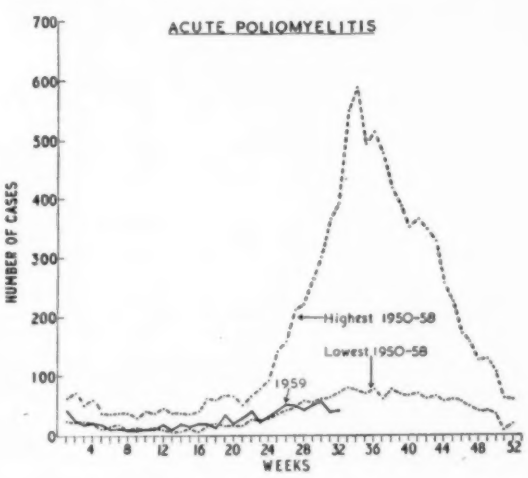
The incidence of poliomyelitis in the U.S.A. is higher than it has been since 1956. The cumulative totals up to the end of the first week in August are shown below.

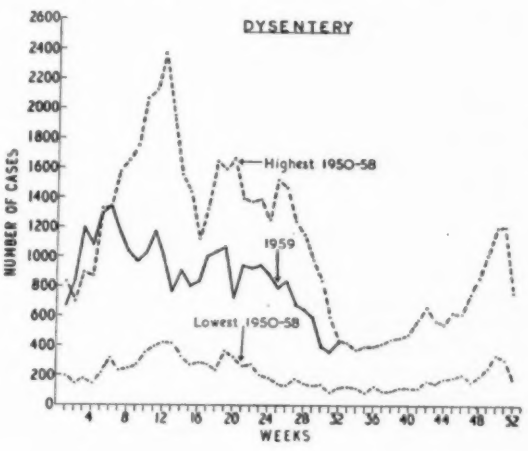
	1955	1956	1957	1958	1959
Paralytic poliomyelitis ..	3,049	2,646	904	579	1,580
Total cases notified as poliomyelitis	7,944	5,330	2,565	1,211	2,482

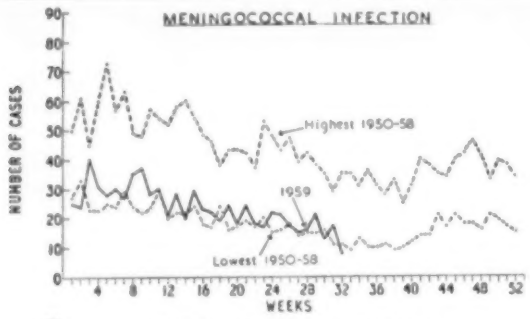
The largest outbreaks this summer have been in the states of Iowa, Missouri, and Arkansas. In some of these outbreaks about 15% of the paralytic cases had received three or more injections of killed vaccine.

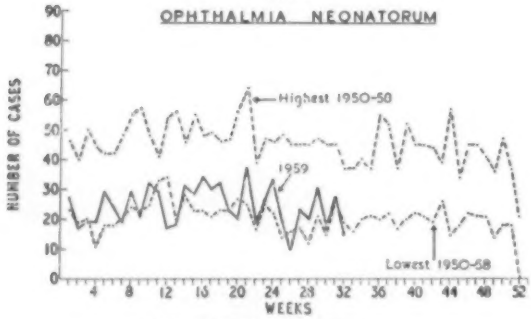
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1950–8 are shown thus ------, the figures for 1959 thus ———. Except for the curves showing notifications in 1959, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Week Ending August 15

Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures were available

	Week Ending Aug. 8	Aug. 15
Measles		
Gloucestershire	71	**125**
Bristol C.B.	47	**66**
Staffordshire	188	**242**
Stoke-on-Trent C.B.	41	**57**
Yorkshire West Riding	309	**341**
Sheffield C.B.	57	**54**
Spenborough M.B.	44	**45**
Dysentery		
Gloucestershire	4	**50**
Thornbury R.D.	0	**46**
London	27	**51**
Deptford	3	**10**
Yorkshire East Riding	15	**41**
Kingston-upon-Hull C.B.	11	**16**
Haltemprice U.D.	2	**24**
Yorkshire West Riding	31	**39**
Thorne R.D.	0	**11**
Glasgow	111	**135**
Acute Poliomyelitis		
London	5	**9**
Islington	2	**3**
Middlesex	7	**4**
Lancashire	1	**7**
Food-poisoning		
Lancashire	53	**76**
Blackpool C.B.	25	**21**
Infective Encephalitis		
Lancashire	0	**3**
Blackpool C.B.	0	**2**
Typhoid Fever		
Kent, Dover M.B.	0	**1**
London, Stepney	0	**1**
Yorkshire West Riding	1	**1**
Conisbrough U.D.	0	**1**
Londonderry County	0	**3**
County Down	0	**1**

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **August 8** (No. 31) and corresponding week 1958.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1959 Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	1958 Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	2	0	2	4		4	0	1	0	
Dysentery	365	27	161	13	3	536	71	132	9	
Encephalitis, acute	0	0		0		5	0		0	
Enteric fever:										
Typhoid	3	0	0	1		1	1	0	0	
Paratyphoid	3	0	2(B)	2	1(B)	9	0	3(B)	0	
Food-poisoning	250	34	20	3		261	24	8	3	
Infective enteritis or diarrhoea under 2 years				12	23				8	31
Measles*	4,598	117	65	99	51	6,299	461	91	30	33
Meningococcal infection	17	3	13	2	1	11	3	8	0	2
Ophthalmia neonatorum	27	2	11	0		32	4	2	0	
Pneumonia†	130	8	80	3		168	12	103	2	1
Poliomyelitis, acute:										
Paralytic	23	5	0	0	2	37	3	26	0	10
Non-paralytic	17	0	3			28	2			
Puerperal fever§	182	40	7	2		202	28	10	0	1
Scarlet fever	463	24	43	11	9	552	44	40	5	12
Tuberculosis:										
Respiratory	353	27	56	11		454	46	90	21	
Non-respiratory	53	6	10	3		63	5	14	5	
Whooping-cough	614	32	99	14	64	709	26	38	39	16

DEATHS	1959 Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	1958 Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	1
Dysentery	0	0		1		0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	6	0	1	0	0	4	1	0	0	1
Influenza	5	1	0	0	0	4	0	0	0	0
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		0	0				0	0		
Pneumonia	298	23	5		7	270	17	10	11	4
Poliomyelitis, acute	3	0		0	0	3	1		1	0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	42	4	5	0	2	64	5	3	1	2
Non-respiratory		0	3	0	0		0	0	0	0
Whooping-cough	0	0	0	0	0	0	0	0	0	0
Deaths 0–1 year	266	21	28	5	4	284	24	13	1	14
Deaths (excluding stillbirths)	7,462	569	433	96	118	8,203	638	482	112	143
LIVE BIRTHS	13,430	1134	1013	229	357	13,970	1180	854	203	334
STILLBIRTHS	293	21	21			303	25	20		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Interdepartmental Committee on Drug Addiction.—This Committee, of which Sir RUSSELL BRAIN is chairman, was appointed on June 3, 1958, with the following terms of reference: "To review, in the light of more recent developments, the advice given by the Departmental Committee on Morphine and Heroin Addiction in 1926; to consider whether any revised advice should also cover other drugs liable to produce addiction or to be habit-forming; to consider whether there is a medical need to provide special, including institutional, treatment outside the resources already available, for persons addicted to drugs; and to make recommendations, including any proposals for administrative measures that seem expedient, to the Minister of Health and the Secretary for Scotland." The Committee decided in the first place to consider evidence from professional and other bodies having experience of or interest in the questions they were investigating. They are now prepared to consider evidence from any other body or person on matters relevant to their terms of reference. A list of particular questions on which the Committee would be willing to consider evidence will be sent on application to the Joint Secretaries, Interdepartmental Committee on Drug Addiction, Ministry of Health, Savile Row, London, W.1.

Pharmaceutical Society's Warning.—The Council of the Pharmaceutical Society has urged pharmacists to discourage the sale of certain drugs which the public can buy without prescription, and which, by stimulating or depressing the nervous system, are peculiarly apt to lead to habit or even addiction. The Society lists the approved names of 28 such drugs and says that "some time-lag between the introduction of new drugs and their sales-control by legislation is probably inevitable, but it is the opinion of the Council that in general these drugs should not be supplied to the public except on medical prescription."—(*Pharmaceutical Journal*, August 22, 1959.)

R.C.P. (Lond.).—At the College's quarterly Comitia on July 30, the following officers were elected for the ensuing year:

Censors: A. M. COOKE, E. R. BOLAND, J. C. HAWKSLEY, K. ROBSON; *Treasurer:* R. R. BOMFORD; *Registrar:* Sir H. E. A. BOLDERO; *Harveian Librarian:* Sir E. CHARLES DODDS, F.R.S.; and *Assistant Registrar:* J. R. ELLIS. Sir FRANCIS FRASER was appointed Harveian Orator and Dr. W. I. CARD Bradshaw Lecturer—both for the year 1960. The following Lecturers were also appointed: *For 1960: Lumleian,* D. EVAN BEDFORD; *Goulstonian,* J. BADENOCH; *Oliver-Sharpey,* J. D. N. NABARRO; *Mitchell,* J. G. SCADDING; *Bertram Louis Abrahams,* H. BARCROFT; *Langdon-Brown,* D. V. HUBBLE. *For 1961: Croonian,* J. MCMICHAEL; *FitzPatrick,* K. D. KEELE; *Watson Smith,* L. FORMAN; *Marc Daniels,* J. C. HOYLE. It was announced that the Ambuj Nath Bose Prize for 1959 had been awarded to Dr. WILSON SMITH, F.R.S., the Baly Medal for 1959 to Dr. I. DE B. DALY, F.R.S., for his outstanding contributions to knowledge of the cardiovascular system and especially of the pulmonary circulation, and the Bisset Hawkins Medal for 1959 to Dr. PERCY STOCKS, for his long series of statistical and epidemiological contributions to the study of disease. The Murchison Scholarship for 1959 had been awarded to Dr. J. H. TURNER. The following were admitted Members of the College: J. M. ANGELONI, J. M. COSTELLO, J. M. EVANSON, O. P. GALPIN, D. R. GANDER, Captain R. GRAHAME, S. G. GROVES, R. HALL, W. B. HANLEY, M. D. A. HELLER, J. G. HUMBLE, J. P. INGHAM, D. C. JACKSON, L. S. LANGE, J. P. LAVENDER, A. O. O. LUCAS, B. B. MACGILLIVRAY, C. DE S. MUTUCUMARANA, J. L. H. O'RIORDAN, M. S. OWEN, H. K. PAL, B. L. PENTECOST, A. I. SCOTT, G. E. SOWTON, R. E. STEINER, N. L. STEPHENS, R. STEPHENS, P. B. STOREY, G. R. THOMPSON, T. M. VANIER, J. E. S. VARLEY, M. V. WELLS, I. A. WILLIAMS, J. V. WILLIAMS, D. B. WILSON, A. L. WOOLF, C. B. WYNN PARRY, and R. T. T. YOUNG.

B.M.A.'s Agar Street Building.—Before the British Medical Association moved to its present home in Tavistock Square in 1925 it occupied a building on the corner of Agar Street and the Strand erected for the Association in 1907–8. Sir JACOB EPSTEIN, the sculptor, who died last week,

aged 78, carved on the stonework of the new facade 18 figures which, in his own words, were meant to represent "the great primal facts of men and women . . . figures joyous, energetic, and mystical." The new building with the sculptor's scaffolding in position is shown here. To-day, the "noble and heroic forms" which the sculptor created are broken and mutilated.

Animal Experiments.—Nearly three and a quarter million experiments were carried out last year on living animals, but 2,879,383 (about 89%) did not require anaesthetics, being inoculations, modifications of diet or environment, or other experiments in which it was unnecessary for the animal to be anaesthetized. In 324,000 experiments, operative procedures, many of a minor nature, were carried out under anaesthesia, from the influence of which, when the operation was completed, the animal was allowed to recover. Experiments performed under anaesthesia in which the animal was killed before recovering consciousness totalled 42,607. In the course of cancer investigations 47,017 experiments were performed under anaesthesia, and in 173,959 without, since they were simply injections, external applications, or feeding experiments designed to exclude the presence of carcinogens in food or other substances in common use. Over a million experiments were performed in standardizing sera, vaccines, or drugs (*Experiments on Living Animals,* Return to Parliament, July 29, 1959).

Harveian Society of London.—The Buckston Browne Essay Prize, consisting of a medal and £100, will be awarded for the best essay on "Iatrogenic Disease." The prize is open to any member of the medical profession registered in the British Isles or Dominions, and is limited to candidates under 45 years of age. The closing date for entries is August 31, 1960. Further particulars may be obtained from the Honorary Secretaries of the Society, 11, Chandos Street, Cavendish Square, London, W.1.

"Panminerva Medica."—*Minerva Medica,* which was founded in January, 1909, as an Italian "review of medical science reviews" and has since been joined by a variety of journals and periodicals, is celebrating its fiftieth anniversary with *Panminerva Medica,* a new monthly review in English

of Italian medicine. The first issue appeared in May, the editor being Professor T. OLIARO, and the assistant editor Dr. G. SCEVOLA. Inquiries and subscriptions (£3 10s.) should be sent to Panminerva Medica, 83, Corso Bramante, Torino, Italy.

Ionizing Radiations Panel.—A panel of 23 experts has been set up under the aegis of the Ministry of Labour's Radioactive Substances Advisory Committee to consider safety and health in relation to the use of ionizing radiations. The chairman of the panel will be Professor B. W. WINDEYER. Among the panel's other members are Professor W. V. MAYNEORD, Dr. E. E. POCHIN, Surgeon Commander F. P. ELLIS, Mr. J. M. JOHNSTON, and Lieutenant-Colonel H. W. WITCHER.

Working Party on Special Hospitals.—The membership of the Working Party has now been completed by the appointment of Dr. D. H. H. THOMAS, medical superintendent of Cell Barnes Hospital, who was a member of the Royal Commission on the law relating to mental illness and mental deficiency. The names of the other 11 members were announced by the Minister of Health on July 30 (*Journal*, August 15, p. 197).

Occupational Health Courses.—The Ministry of Health has recently decided that postgraduate courses in occupational health can be provided under section 48 of the N.H.S. Act. Two such courses have already been arranged: one at the London School of Hygiene and Tropical Medicine (September 28–October 3), and another at the Nuffield Department of Occupational Health at Manchester University (November 2–7). More will be made available if there is a demand for them. Further details obtainable from the Registrar, London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1.

Faculty of Anaesthetists, R.C.S. (Eng.).—Dr. GEOFFREY ORGANE has been re-elected dean, and Professor E. A. PASK vice-dean, of the faculty for the coming year. Dr. ASHLEY DALY, consulting anaesthetist to the London Hospital, has been admitted to the faculty's honorary fellowship.

London's First M.O.H.—A plaque commemorating London's first medical officer of health, Sir JOHN SIMON, has been put up outside 40, Kensington Square, where he lived for 37 years. He died, aged 88, in 1904.

J.A.M.A.'s New Editor.—Dr. JOHN H. TALBOTT, professor of medicine, University of Buffalo School of Medicine, has been appointed editor of the *Journal of American Medical Association* and director of the A.M.A.'s Division of Scientific Publications. Professor Talbott succeeds Dr. JOHNSON F. HAMMOND, who succeeded less than twelve months ago Dr. AUSTIN SMITH, who resigned after being nearly ten years in the editorial chair in succession to Dr. MORRIS FISHBEIN, who gave up his office in 1949 following a disagreement with the A.M.A.'s Board of Trustees. We wish Professor Talbott all success in his new career.

COMING EVENTS

Nutrition Society (Scottish Group).—Symposium, "Nutrition at the Cellular Level," Aberdeen, September 19. Details from Dr. J. DAVIDSON, The Rowett Research Institute, Bucksburn, Aberdeen.

Journées Gynécologiques et Obstétricales de Lisbonne.—Lisbon, Portugal, September 19–22. Details from Dr. MARIO CARDIA (U.P.I.G.O.), 98, Rua Anibal Cunha, Porto-Portugal.

Institute of British Surgical Technicians.—A course of lectures on "The Anatomy, Pathology and Treatment of Hernia" will be given weekly from September 22, at 7 p.m., at Bolton Technical College, Manchester Road, Bolton. Details from the Registrar of the Institute, 6, Holborn Viaduct, London, E.C.1.

Psychotherapy in General Practice.—Seminars for general practitioners will be conducted by Dr. GRAHAM HOWE at the Open Way Psychotherapy Clinic, fortnightly on Tuesdays from 3 to 4 p.m., from September 22 to July, 1960. Details from the Secretary, The Open Way, 37, Queen Anne Street, London, W.1 (LAN 1941).

8th Congress of International Union of Railway Medical Services.—September 21–26, Lucerne. Details from Dr. ORTEGA, 13, rue de Château-Landon, Paris, 10, France.

Epsom College.—Extraordinary General Meeting of the College Governors to appoint a President in succession to the late Lord WEBB-JOHNSON, Council Room, Medical Defence Union, Tavistock House South, Tavistock Square, London, W.C.1, September 25, 4 p.m.

Glasgow Postgraduate Course.—A course of clinical teaching ward rounds will be held in Glasgow hospitals on Thursday afternoons, 4.30 p.m., from October 8. Last date for application is September 17. For details see this week's *Journal*, advertisement page 49.

NEW ISSUES

SPECIALIST JOURNALS AND ABSTRACTS

The Journals listed below are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

Archives of Disease in Childhood.—Issued six times a year (£4 4s. annually). The new issue (Vol. 34, No. 175) includes:

EDITORIAL NOTE
BRONCHIECTASIS IN CHILDREN. ITS MULTIPLE CLINICAL AND PATHOLOGICAL ASPECTS. Howard Williams and R. N. O'Reilly.
RESPIRATORY STRIDOR PRODUCED BY AN ABERRANT PULMONARY ARTERY. W. H. Schuit and P. M. Robb.
BONE LESIONS OF URTICARIA PIGMENTOSA IN CHILDHOOD. Martin H. Lees and C. Eric Stroud.
A LONGITUDINAL STUDY OF THE GROWTH AND DEVELOPMENT OF PREMATURELY AND MATURELY BORN CHILDREN. PART IV. MORBIDITY. Cecil Mary Drillien.
A CASE OF IDIOPATHIC PULMONARY HAEMOSIDEROSIS WITH MYOCARDITIS. S. Campbell and C. A. J. Macafee.
CONGENITAL HEART BLOCK. R. W. Smithells and E. B. Outon.
CONGENITAL ANOMALIES ASSOCIATED WITH CEREBRAL PALSY AND MENTAL RETARDATION. Ronald S. Illingworth.
HYDRANENCEPHALY AND ALLIED DISORDERS. C. S. Muir.
INCIDENCE OF RHEUMATIC FEVER IN CEYLON. Stanley de Silva.
HERPES SIMPLEX VIRUS INFECTION: DISSEMINATION IN ASSOCIATION WITH MALNUTRITION. D. McKenzie, J. D. L. Hansen, and W. Becker.
CHRONIC ULCERATIVE COLITIS IN CHILDHOOD. Donald C. King, Arthur E. Lindner, and H. Marvin Pollard.
PHYSIOLOGICAL JAUNDICE. A. A. Cunningham.
THE DIAGNOSIS OF MENTAL RETARDATION IN INFANCY. R. S. Illingworth and L. B. Birch.
CONGENITAL HYDROCEPHALUS IN MONOVULAR TWINS. V. Gellman.
A CASE OF RUPTURE OF THE HEPATIC DUCT IN A NEWBORN INFANT. Joan P. Wright and Helen E. Worsley.
BOOK REVIEWS.

Abstracts of World Medicine.—Issued in the first week of each month, this journal contains abstracts of important papers selected from the current medical literature of the world. Annual subscription £4 4s.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Thursday, September 3

MIDDLESEX HOSPITAL.—At Courtauld Lecture Theatre, 5.15 p.m., Professor A. Gorman Hills (Miami University): Some Aspects of Adrenal Deficiency.

Friday, September 4

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. Howard Nicholson: clinical demonstration.

BIRTHS, MARRIAGES, AND DEATHS

DEATHS

Barker.—On June 30, 1959, at Silverstream, Headbourne Worthy, Winchester, Hants, Frederic Allan Barker, C.I.E., O.B.E., M.D., Lieutenant-Colonel, I.M.S., retired, aged 76.

Brookes.—On June 30, 1959, at 75, Commercial Road, Kirkstall, Leeds, 5, Philip Brookes, T.D., L.M.S.S.A., aged 62.

Church.—On June 26, 1959, at Blairgowrie Cottage Hospital, Duncan Macdonald Cochrane Church, M.B., Ch.B., Major, I.M.S., retired.

Dorrell.—On June 23, 1959, at King Edward VII Hospital for Officers, London, W., Edmund Arthur Dorrell, F.R.C.S., D.P.H., of 76, Bryanston Court, London, W., aged 87.

Duggan.—On June 26, 1959, Michael Duggan, M.D., of Brantford, Ontario, Canada, aged 39.

Fairweather.—On June 26, 1959, at Royal Cornwall Infirmary, Truro, Joseph Hayes Fairweather, M.D., D.P.H., D.M.R.E., of Clitheroe, Lancs.

Franey.—On June 24, 1959, after an operation at Plymouth, Roy Francy, M.R.C.S., L.R.C.P., D.P.H., F.R.I.C.S.

Lewis.—On June 26, 1959, at Dormers, Wimborne, Dorset, Herbert Wolseley Lewis, M.D., F.R.C.S., aged 90.

Seccombe.—On June 30, 1959, at his home, Matatiele, East Griqualand, C.P., South Africa, Sidney Thomas Seccombe, M.B., B.S., D.P.H., formerly of Ringwood, Hants.

Teale.—On August 22, 1959, Sir Francis Hugo Teale, K.C.V.O., M.D., F.R.C.P., of 32, Harley House, London, N.W.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Pseudomonas pyocyaneus Cystitis

Q.—*A patient has recurrent cystitis after prostatectomy. Culture shows a heavy growth of Pseudomonas pyocyaneus, which is resistant to penicillin, streptomycin, and sulpha drugs. What treatment would clear the infection?*

A.—*Pseudomonas pyocyaneus* is probably the most resistant organism causing urinary infections. Many of its strains are resistant to all the known antibiotics and sulpha drugs. Polymyxin is the most active of the antibiotics, but is regarded as too toxic for general use. Chloramphenicol and oxytetracycline are the next most effective against the various strains of this organism. It is therefore essential to have the organism typed against all the antibiotics and sulpha drugs, so that the most active may be used. If the organism is resistant to all these drugs, a short period of cessation of all urinary antiseptics may allow the pyocyaneus to be displaced by some other organism, such as *B. coli*, which is more amenable to treatment. Irrigation of the bladder with acetic acid in strengths of 1 in 500 to 1 in 100 has been successful when oral medication has failed. But more important than eliminating the pyocyaneus is to establish the cause of the recurring cystitis and the persistence of this organism. Before further treatment is undertaken an investigation should be instituted to exclude the presence of residual urine due to post-prostatectomy obstruction, ragged prostatic cavity, stones in the bladder, or a diverticulum of the bladder, which can be done by an intravenous pyelogram and, if necessary, a cystoscopy.

Thoracic Outlet Syndrome

Q.—*What is meant by the "thoracic outlet," the "thoracic inlet," and the "axillary inlet" syndromes? Are they the same thing?*

A.—The "thoracic outlet," "thoracic inlet," and "axillary inlet" syndromes are the same. They are due to compression, in a variety of ways, of the neurovascular bundle as it passes from the neck to the arm. Thus it may be found in association with cervical rib; it may occur without any bony abnormality, owing to compression between the clavicle and the first rib; it may occur as a result of abnormal action of the scalenus anticus muscle; it is sometimes due to pinching of these structures when the arm is elevated—the hyperabduction syndrome; and, lastly, the compression may occur between the clavicle and the first rib as the shoulder joint is rotated outwards and decompressed. This latter is sometimes known as the costoclavicular syndrome.

To-day the thoracic outlet and the other two syndromes named are taken to include all the above abnormalities.

Alcoholic Drinks for Children

Q.—*Should children be allowed to drink half a pint daily of a beverage containing 6% alcohol by weight?*

A.—This is a formidable brew and twice as strong as the average beer. Half a pint of it, containing 17 g. of alcohol, if taken over a short period of time by a child 10 years of age would give a blood alcohol of about 60 mg. per 100 ml., and this would certainly lead to some disturbance of behaviour. Spread in small doses over the day it is doubtful if this amount of alcohol would give rise to more than a little lowering of the threshold of emotional response or possibly to mild sedation. Half a pint of this beverage is roughly equivalent to a quarter of a bottle of claret, and there must be large numbers of children in France, Italy, Spain, and Portugal who habitually take this amount of wine without conspicuous ill effect and certainly without becoming chronic alcoholics. One's views are largely coloured by one's attitude to the consumption of alcohol in general. I should not myself regard its consumption by children as a desirable practice.

Leprosy in U.K.

Q.—*What was the number of cases of leprosy in the United Kingdom in 1940, 1950, and 1958? How many centres are there for the treatment of this disease?*

A.—No information is available on the incidence of leprosy in England and Wales before 1951, when the Public Health (Leprosy) Regulations, 1951, were introduced. In that year there were 46 notifications and there were 44 in 1958, bringing the total number of cases up to 273 to the end of the year. In none of the cases was the infection contracted in the United Kingdom. There are two special centres for the treatment of the disease, one in Surrey, the other in Essex. In certain types of case treatment is given at various dermatological clinics throughout the country after consultation with the specialist adviser to the Ministry of Health.

In Scotland leprosy became notifiable at the beginning of 1951 and there are therefore no figures available for 1940 and 1950. The number of notifications in Scotland in 1951 was 5 and in 1958 the figure was 4. Treatment may be undertaken at any of the major infectious diseases hospitals in Scotland, but the two larger hospital regions find it convenient to concentrate cases in selected units.

Leprosy is not notifiable in Northern Ireland, and there are no centres for treatment there. About the end of the war a West Indian student at a university developed the disease, and after diagnosis he returned to his own country. The Army notified a case of a soldier in February, 1954. The disease had been acquired abroad, and the Army dealt with the case. The Ministry of Health has no record of any cases in 1940, 1950, or 1958.

Inheritance in Infantile Eczema

Q.—*A boy aged 2½ suffers from allergic eczema. What is the likelihood of any future brothers or sisters being affected, and is there any sex differentiation?*

A.—The chance of infantile eczema recurring in later brothers or sisters is well above the random risk, but not high. No directly relevant published series is known to me, but a personal series indicates that the risk is probably less than 1 in 20. The risk is probably rather higher for a brother than a sister. In addition to infantile eczema the later brothers and sisters have a small but definite increase in the risk of other allergic disorders—urticaria, asthma, and hay-fever.[1]

REFERENCE

[1] Edgren, G., *Acta paediat.*, 1943, **30**, suppl. 2.

Treatment of Sinusitis

Q.—*What are recent views on the treatment of sinusitis and its prevention?*

A.—Sinusitis is usually due to a spread of infection from the nasal passages up into the sinuses. Considering the frequency of acute nasal infections and the easy opportunities for spread into the sinuses, it is a tribute to the general and local defences of the body that sinusitis is such a relatively infrequent complication of a head cold. Sinusitis may also follow bathing, particularly if a head cold is present, and in the case of the antrum a dental infection may spread from an adjacent upper premolar or molar tooth.

In sinusitis secondary to a head cold the infecting organism is usually a streptococcus or pneumococcus, and antibiotic therapy plus measures to maintain a good nasal airway, such as steam inhalations, will usually effect a cure. In the case of the maxillary sinus puncture and lavage of

the sinus via the inferior meatus may be needed. These measures, if properly applied, rarely fail to effect a cure, and operations for drainage of the frontal or maxillary sinuses are rarely called for nowadays.

Recurrent sinusitis may be due to interference with the normal drainage by a deflected septum, which will need surgical correction in a quiescent period, and nasal polypi will have to be removed also when the acute infection has subsided. An unusually large middle turbinal may obstruct free drainage from the frontal and maxillary sinuses, in which case it will need to be removed. When there is a history of recurrent sinus infection with head colds consideration should be given to a course of autogenous vaccine prepared from the patient's nasal and pharyngeal secretions. Though this may not prevent the primary virus infection responsible for a head cold, it will discourage the development of secondary infections, such as sinusitis, from organisms already present in the nasal passages. Patients with such a history should always be prepared to take a head cold seriously, to rest in a warm atmosphere for 48 hours, inhale steam frequently, and if necessary to take a short course of antibiotic or sulphonamide therapy.

Poliomyelitis Vaccination after Gamma Globulin Injection

Q.—*A patient who is expecting her first baby on December 10 was exposed to rubella on April 19. She received 1,500 mg. gamma globulin on April 21. When should her first and second poliomyelitis injections be given?*

A.—The gamma globulin might well contain antibodies to poliomyelitis, and these might interfere with the patient's response to a first dose of poliomyelitis vaccine. At the end of three weeks these antibodies would either have disappeared or be at a level unlikely to interfere with the patient's response to active immunization. The first dose of poliomyelitis vaccine should therefore be given around May 20 and the second one month later.

NOTES AND COMMENTS

Gout and Disk Lesions.—Dr. J. L. BRAITHWAITE (Liverpool) writes: I was most interested in the question posed, "Is there any relationship between gout and disk lesions?" and the answer given by your expert ("Any Questions?" June 27, p. 1622). Had the question been phrased, "Is there anything in common between gout and disk lesions?" the answer should most certainly have been in the affirmative, for in both conditions the pain in the acute phase can only be described as "exquisite." I can speak from personal experience of both, having been treated for a "slipped disk" in 1948 to be followed by periodic attacks of gout which commenced in the spring of the following year and have persisted in mild form since, occurring in both the spring and autumn ("in rhythm with the rise and fall of the sap"). The alleged disk lesion, in the joint opinion of four distinguished consultants (three orthopaedic surgeons and one physician), could not be attributed to any of the generally accepted predisposing factors but commenced suddenly as an acute pain—in the lumbar area—in bed, in the small hours of the morning. It responded within a week to rest and sedatives. The following year brought in its wake a pain of similar severity, though transposed to the left ankle joint. It was treated originally as a "trapped tag of synovial membrane," first in "elastoplast" followed by plaster of Paris (although it is difficult in retrospect to understand by what mechanism such a lesion could be produced during sleep). A far-seeing colleague of mine suggested that a serum uric acid estimation might be worthy of trial. This investigation proved beyond doubt that the correct diagnosis was acute gout. Colchicine then and since has been of inestimable value in the treatment. The family history, on careful scrutiny at a later date, showed that both my father and paternal grandfather had suffered from "periodic attacks of rheumatism in the feet." More recently the advent of tophi in the auricle has afforded conclusive proof of the condition. In the light of past experience and the great personal interest I have taken in "fully proved" gout sufferers (this is perhaps because there is no stronger medical fellowship than that which binds together in a common sympathy the hardened warriors of these disordered metabolic campaigns), I should like to make three general observations: (1) Gout can affect any joint. It does not by any means always involve the so-called weight-bearing joints. It is, however, generally accepted that the big toe joint is the one most commonly involved. This poses something of a paradox, because the main weight-bearing area of the foot is on the post-axial or little toe side and not on the pre-axial or big toe side. Gout affecting joints on or near the post-axial border is much less common than on the pre-axial side. (2) If weight transmission to the foot is in any way deranged (as in spinal deformity such as lordosis) the excessively angulated joints in the area seem to be involved initially in some instances, prior to the deposit of urates in more distal joints and the appearance of "classical gout." I am convinced in retrospect that the postural deformity of lordosis aided by heredity contributed to an attack of gout in the joints of the lumbar column and not a slipped disk of which it had all the appearances at the time. I have since been convinced of a similar type of history of the advent of gout in a few of my fellow sufferers. (3) It might be desirable in the atypical disk lesion (without history of trauma, absence of nerve involvement, etc.) to carry out a serum uric acid estimation, for this might well reveal the first attack of acute gout, labelled incorrectly slipped disk, in which case the appropriate line of treatment so lucidly presented in a recent article in "Drug Treatment of Disease" (*Journal*, June 13, p. 1522) could be instituted without delay. There are many authorities who have contributed much enlightenment on the subject of gout, and I do not count myself among them. My only qualification for comment is that, just as an individual who is or has been married is in my opinion best suited to write on the subject of marriage, so I feel a gout sufferer of ten years' standing (not strictly accurate) is equally eligible to air his views on those "exquisite metabolic interludes" considered to be both humorous and self-inflicted by one's friends, an irritable episode for one's wife, and so inaptly originating from "gutta"—a drop.

Dr. T. D. DAY (Leeds, 2) writes: The negative answer to the question as to the relationship between gout and disk lesions ("Any Questions?" June 27, p. 1622) is not, I think, entirely correct. It is true that gout is a metabolic disease and that the proximate cause of pain in disk lesions is purely mechanical, but surely one must also take into consideration those conditions which make displacement of a disk likely. There can be no doubt that one of these is the chemical composition of the tissue fluid, since it has been shown that connective tissue structures react to very slight changes in chemical environment by swelling or shrinking. It may be empirically true that gout and disk lesions are not usually associated, but the reasons for this are not as self-evident as the answer given would suggest. What prompted me to write this letter was my personal experience that an attack of acute articular gout is usually preceded or accompanied by root pains which I have always thought to be due to swelling of the cervical disks.

OUR EXPERT replies: The letters published above raise an important point with regard to the association of metabolic changes, such as occur in gout, and disk lesions. There is a possibility that chemical changes in tissue fluid and possibly in the disks themselves may play a part in the aetiology of the "prolapsed" disk. Although this is an interesting theoretical conception, which may one day be proved to be correct, there is as yet little scientific evidence to support it.

Collected Articles from the "British Medical Journal"

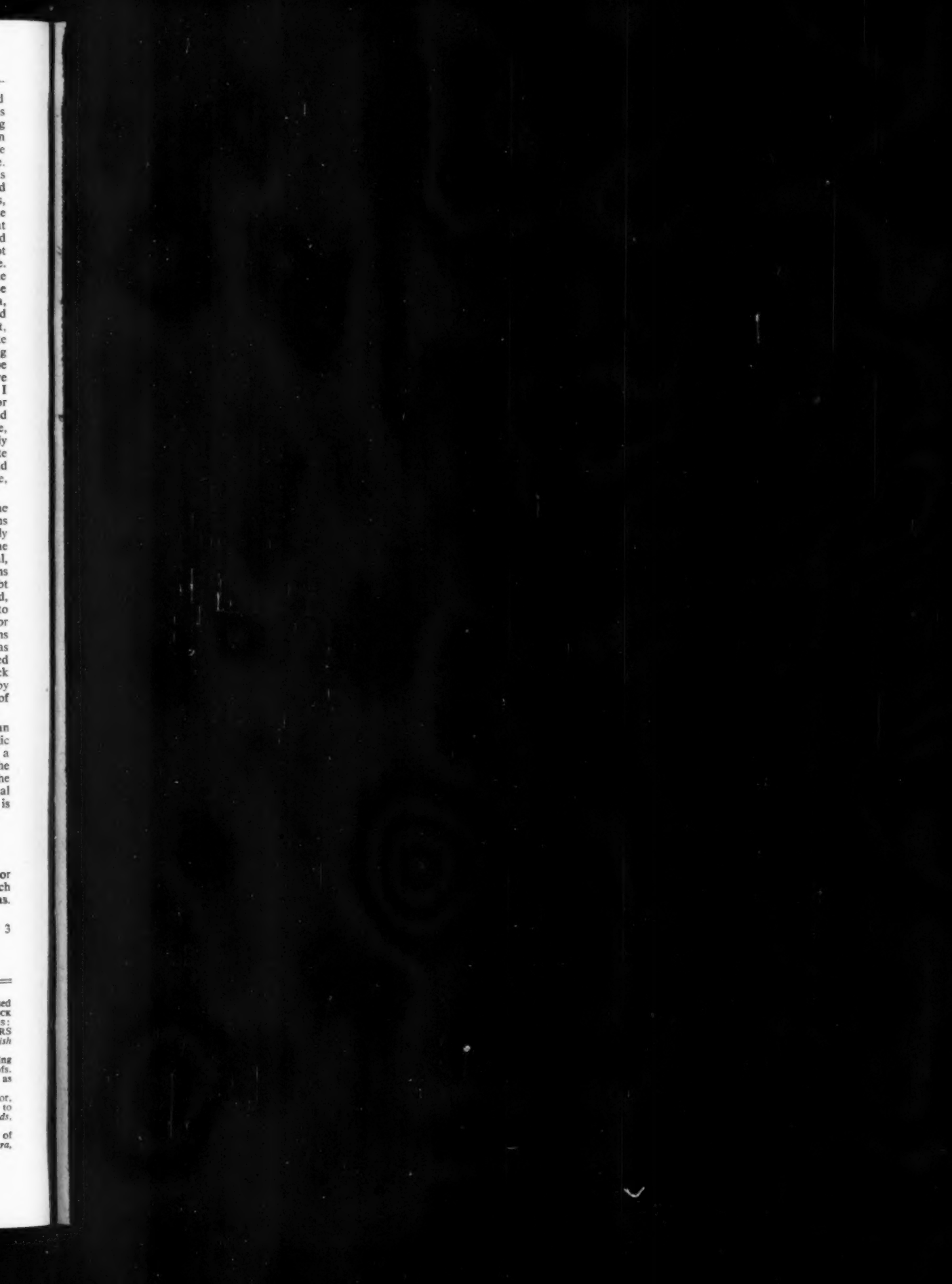
The following books are available through booksellers or from the Publishing Manager, B.M.A. House. Prices, which include postage, are now the same for both inland and overseas.

Emergencies in General Practice (26s. 9d.),
Refresher Course for General Practitioners, Volumes 2 and 3 (26s. 9d. each).
Clinical Pathology in General Practice (22s. 3d.).
Any Questions?, Volumes 2 and 3 (8s. 3d. each).

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs. Authors overseas should indicate on MSS. if reprints are required, as proofs are not sent abroad.

ADVERTISEMENTS should be addressed to the Advertisement Director, B.M.A. House, Tavistock Square, London, W.C.1 (hours 9 a.m. to 5 p.m.). TELEPHONE: EUSTON 4499. TELEGRAMS: *Britmedads, Westcent, London.*

MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the Association. TELEPHONE: EUSTON 4499. TELEGRAMS: *Medisecra, Westcent, London.*

B.M.A. SCOTTISH OFFICE: 7, Drumsheugh Gardens, Edinburgh.